

# THE BRITISH JOURNAL OF TUBERCULOSIS

EDITED BY  
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# THE BRITISH JOURNAL OF TUBERCULOSIS

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## EDITORIAL

AMID the tempests of war it is hard to keep abreast of new achievements, especially in those spheres whose importance is far removed from current events. But to reflect on old problems with new material at such times not only refreshes the mind, but evokes something of that perspective which is just and necessary to the estimate of enduring things. Knowledge of the anatomical development of human tuberculosis can fairly claim this rank.

Last August the *American Review of Tuberculosis* published as a supplement\* a volume of studies on this subject. It is a detailed monograph comprising the results of eight years of work on nearly a thousand examples of tuberculous disease, and it is written by a former pupil of Anton Ghon. It is stamped throughout with the warrant of patient care and prolonged thought.

Kornel Terplan has no illusions about the difficulties of adding to our knowledge of the natural history of tuberculosis. The only stage upon which general agreement has been reached so far is the primary focus. The characteristics of this lesion and the fact that an initial infection with the tubercle bacillus in man always behaves in the same way regardless of the portal of entry are accepted almost with the veneration of dogma. This is true not only as regards the lungs and intestinal tract, but also for such unusual localisations for the primary focus as the middle ear, tonsils, nasal passages, and conjunctivæ. No such agreement about later lesions has so far been possible. Many obstacles bar the way—the vast amount of labour entailed in the necessary dissections and histological studies, the differing forms of necropsy material available in various countries, and not least the difficulty of correct interpretation.

\* Terplan, K., "Anatomical Studies on Human Tuberculosis." *Amer. Review Tuberculosis*, 1940, 42, No. 2, Supplement.

In opening his account Terplan defines his use of terms. He deprecates a fashion to allow the term "primary focus" to be used as a cover for lesions other than the initial localisation, and rightly insists that calcification in a particular focus is no proof whatever that such a focus forms part of a primary complex. In the field of post-primary tuberculosis he confines use of the term *reinfection* to its strictest sense of a new infection with tubercle bacilli from an external source; and he replaces *endogenous reinfection*—a contradiction in terms—by *endogenous exacerbation*. Secondary complications of a primary tuberculous pneumonia or bronchogenic or hæmatogenous extension are wrongly designated if regarded as due to endogenous reinfection or superinfection. The term *reinfection* properly defines a new clinical manifestation or anatomical lesion occurring in an individual who already has an old primary lesion; and it presumes a free interval between the time of first infection and the second manifestation. Myers regarded the tuberculin reaction as the best guide in defining this state of reinfection, but Terplan points out once again that as sensitivity develops soon after the primary infection takes place and in an early stage of the period during which the primary complex is formed, the distinction between those lesions which result from a first infection (so called "childhood type") and those which result from true reinfection (so called "adult type") depends more upon anatomical than upon immunological criteria. The wide differences between the two forms cannot be explained so readily, as Pinner, Miller, and others have pointed out already, and, moreover, primary tuberculosis is not always acquired during childhood, a point which recent work has been emphasising increasingly among certain communities. Adults may very well show the striking lesions of a first infection, further evidence for which Terplan brings together in this monograph.

The chief merit of Terplan's work is that it illuminates better than has been done for some time the confused mass of terminology which has been shackling understanding of the subject of tuberculous pathogenesis for the last two decades. He brings evidence that the adult frequently shows a lesion that conforms to the "primary" type, and that the so-called "adult type" is not necessarily the effect of reinfection. He doubts, as indeed most in this country already do, whether it is ever possible to draw a parallel between the anatomical stage of the disease and the allergic features, as Ranke postulated in his original papers.

Turning to the details of his own anatomical work, it is worthy of note that he found no less than six out of thirty examples of acute primary



tuberculosis of the lungs with cavitation of the primary focus. He relates the extensive intrabronchial lesions that were present to this fact. Thus Ghon's original findings are reaffirmed once again, and the belief that has grown up since then that cavities do not occur in primary tuberculosis, or are merely terminal events, has been shown to be erroneous. Primary foci without any histological changes in the related lymph nodes were found in five examples, thrice completely calcified. That true tuberculous reinfection from without may occur in the child as well as in the adult is illustrated by a single instance, where extensive caseation with a meningitis originated from a recent complex in one upper lobe, whilst the other contained an armoured focus the residue of a first infection. This shows that an exogenous reinfection can follow the classical course of a primary tuberculosis with a progressively caseating complex, whilst at the same time the focus due to the first infection remains healed. Bronchial obstruction among children with intrathoracic tuberculosis receives a detailed chapter based upon experience of five patients in which necropsy control was obtained. The primary focus may be the cause if it occludes a secondary or tertiary bronchus, or the intrabronchial extension of an active primary lesion, or again the involvement of regional lymph nodes. Terplan subscribes to the view that pulmonary collapse forms the morphological basis of the massive shadow of epituberculous pneumonia, and that it follows upon complete obstruction of a bronchus. He found nothing in his material to support alternative explanations, and bronchial occlusion was the common factor in all.

Turning to adults, Terplan describes examples of the primary complex in later life and reviews the literature. There comes then an account of ten cases with typical tuberculous complexes of the reinfection type. In all of them the original primary focus was represented by a completely calcified complex that was obviously obsolete. It is clearly shown that the reinfection complex differed in no way from the original one considered to be characteristic of primary tuberculosis exclusively. The same regressive changes with encapsulation and calcification occurred, and the inference is made that the finding of multiple calcified complexes does not necessarily indicate that they are formed simultaneously by a single primary infection.

From this the author goes on to show that a typical recent tuberculous complex due to exogenous reinfection was the source of progressive fatal tuberculosis in two white adults—a picture identical with that so far observed only in primary tuberculosis in children and adults with immediate or

protracted hæmatogenous dissemination. The general path of the argument is illuminated further by sections in which he shows that healed hæmatogenous peritoneal or genital tuberculosis can be followed by a true reinfection with the typical anatomical pattern of a primary intestinal tuberculous complex; that multiple calcified complexes found in adults are not necessarily obsolete primary lesions; and that occasionally only the exogenous reinfection focus in the adult produces the picture typical of a primary complex, while the real primary infection, found in an obsolete state, is restricted to a single parenchymal lesion without evidence of extension to regional lymph nodes. Finally, he shows that the latter point may apply also to a true primary focus found in adult life without other lesions—that, in other words, Parrot's law, like others, is not inviolate.

With this we must leave a fascinating and important study. Terplan's observations, if confirmed, seem likely to dispel much of the prized theory that for two decades has camouflaged the pathogenesis of tuberculosis, and to bring us once again to a conception of an underlying morphological unity in tuberculous processes. Such a view has perhaps always been held by a majority of morbid anatomists, but it has been obscured in recent years since the concepts of immunology and radiology entered the field, and observations, which were interpreted as facts, failed to agree with anatomical teaching. The process turned to theory, and upon foundations of erythemas and shadows a vast and complex architecture came to be built, an architecture which was intelligible to few but zealots. Almost it is true to say that of those most concerned with tuberculosis many have turned from attempts to understand, feeling that until pathologists gave a further guide there was not much to be gained. This careful work of Terplan's does something to light the way, and it is to be hoped that the facts which he has collected and the sensible conclusions which he draws will not be lost upon contemporary opinion.

## GENERAL ARTICLES

## THE ÆTIOLOGY OF SUB-ACUTE PULMONARY INFECTIONS

(A CRITICAL REVIEW OF SOME UNUSUAL CASES)

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## Introduction

THE increasing use of radiography in the diagnosis of pulmonary lesions, and especially in the early detection of pulmonary tuberculosis, is, perhaps, the most outstanding feature of the recent development in our knowledge of this branch of medicine. The importance of X-ray examination of the chest has reference not only to the detection of disease at a stage in which it is unaccompanied by definite physical signs—the significance of the “silent lesion” in pulmonary tuberculosis, for example, is recognised by all competent authorities—but also to the differentiation between various pathological states of the lung in cases in which bacteriological evidence is absent or inconclusive. At the same time it must be admitted that side by side with the clear revelations which it has furnished radiography has brought its own additional problems. Many pulmonary lesions are now brought to light which before the days of adequate X-ray examination passed undetected, and, while in most of these the nature of the disease is not in doubt, in many the differential diagnosis is still a matter of considerable difficulty. In other words, radiological diagnosis, no less than physical diagnosis, has its limitations, nor does it always provide us with a short cut to that understanding of the morbid anatomy of disease which can be reached only by a synthesis of all the available data.

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Such difficulties are well illustrated by the following five cases, which provide material for considerable discussion, and on the ætiology of which we hope that some additional light may be thrown.

### Case Reports

CASE 1.—J. C., female, aged twenty-five, married, had not been feeling well since November, 1936, when she caught a bad cold. On March 9, 1937, she complained of sore throat and felt really ill; her temperature rose to

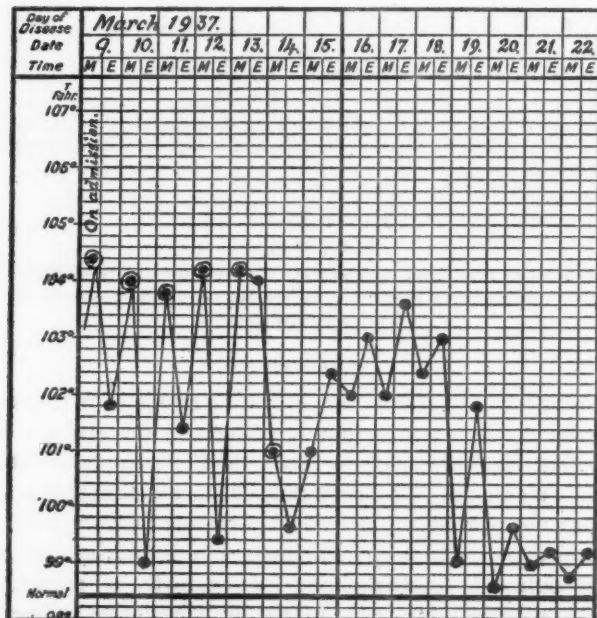


FIG. 1.—TEMPERATURE CHART OF CASE 1, DURING THE FIRST FORT-NIGHT OF ILLNESS.

104.6°, and from this time onwards she had an intermittent pyrexia (see Chart, Fig. 1). Her doctor could find no obvious cause for the fever, and after some days called in a consultant who made various investigations (Widal reaction, blood culture, bacteriological examination of a catheter specimen of urine), with negative results. Three examinations of the sputum for tubercle bacilli were negative. At the end of about ten days suspicious physical signs appeared in the upper part of the chest on the right side, and a portable X-ray examination showed evidence of consolidation in the right upper and middle zones of the lung fields. She was admitted to the Brompton Hospital on March 22 for observation.

PLATE I.

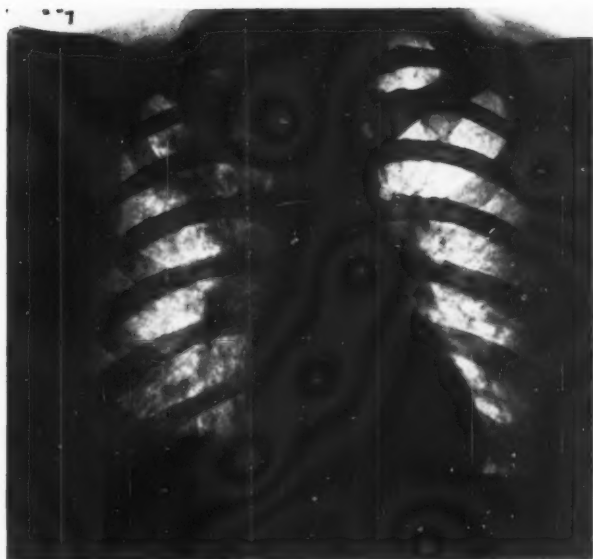


FIG. 2.—RADIOGRAM OF CASE I (23/3/37) SHOWING INFILTRATION OF RIGHT UPPER ZONE.

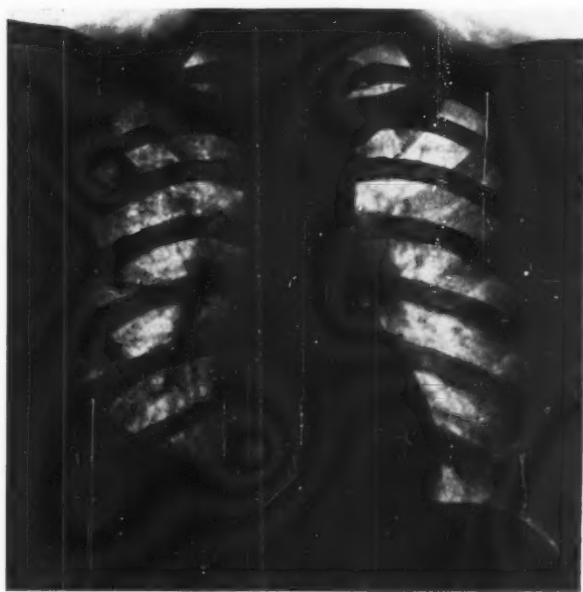


FIG. 3.—RADIOGRAM OF CASE I (13/4/37) SHOWING PARTIAL RESOLUTION.

[To face page 6.

PLATE II.

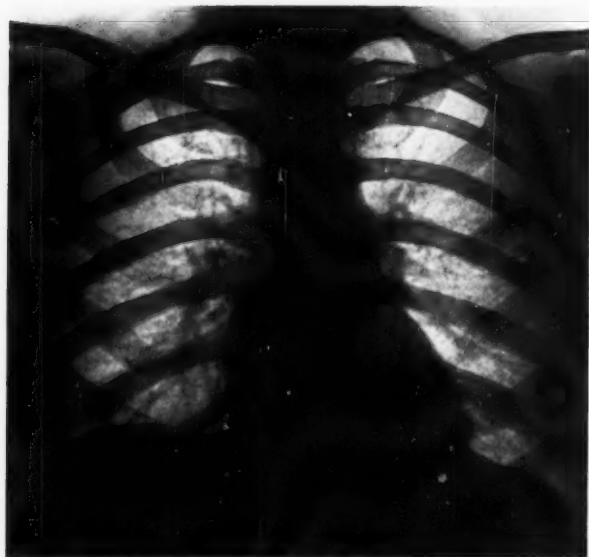


FIG. 4.—RADIOGRAM OF CASE 1 (27/9/37) SHOWING COMPLETE RESOLUTION.

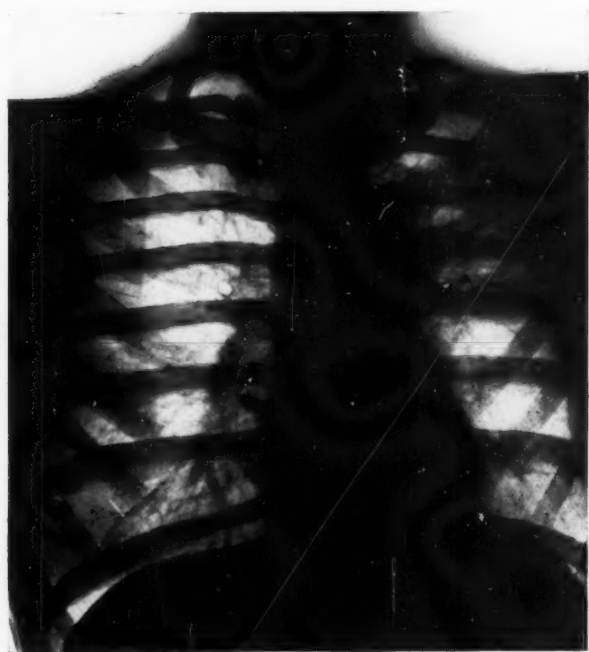


FIG. 5.—RADIOGRAM OF CASE 2 (3/4/40) SHOWING EXTENSIVE INFILTRATION OF THE LEFT UPPER ZONE.

PLATE III.

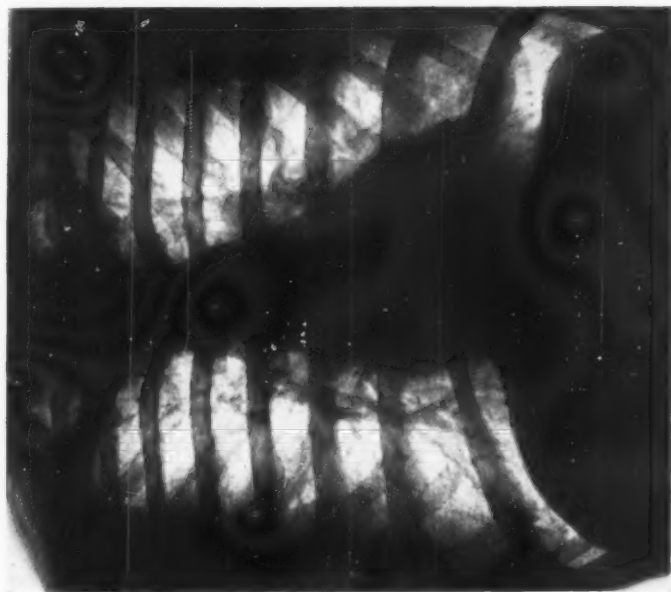


FIG. 6.—RADIOGRAM OF CASE 2 (5/6/40) SHOWING COMPLETE RESOLUTION.

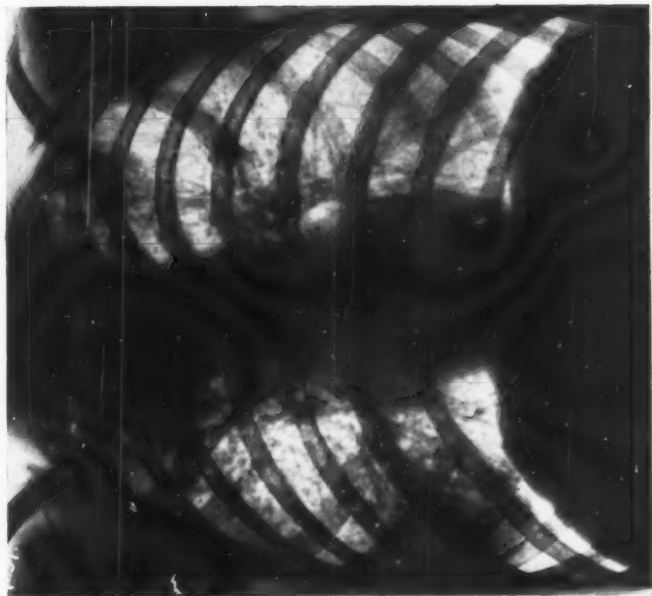
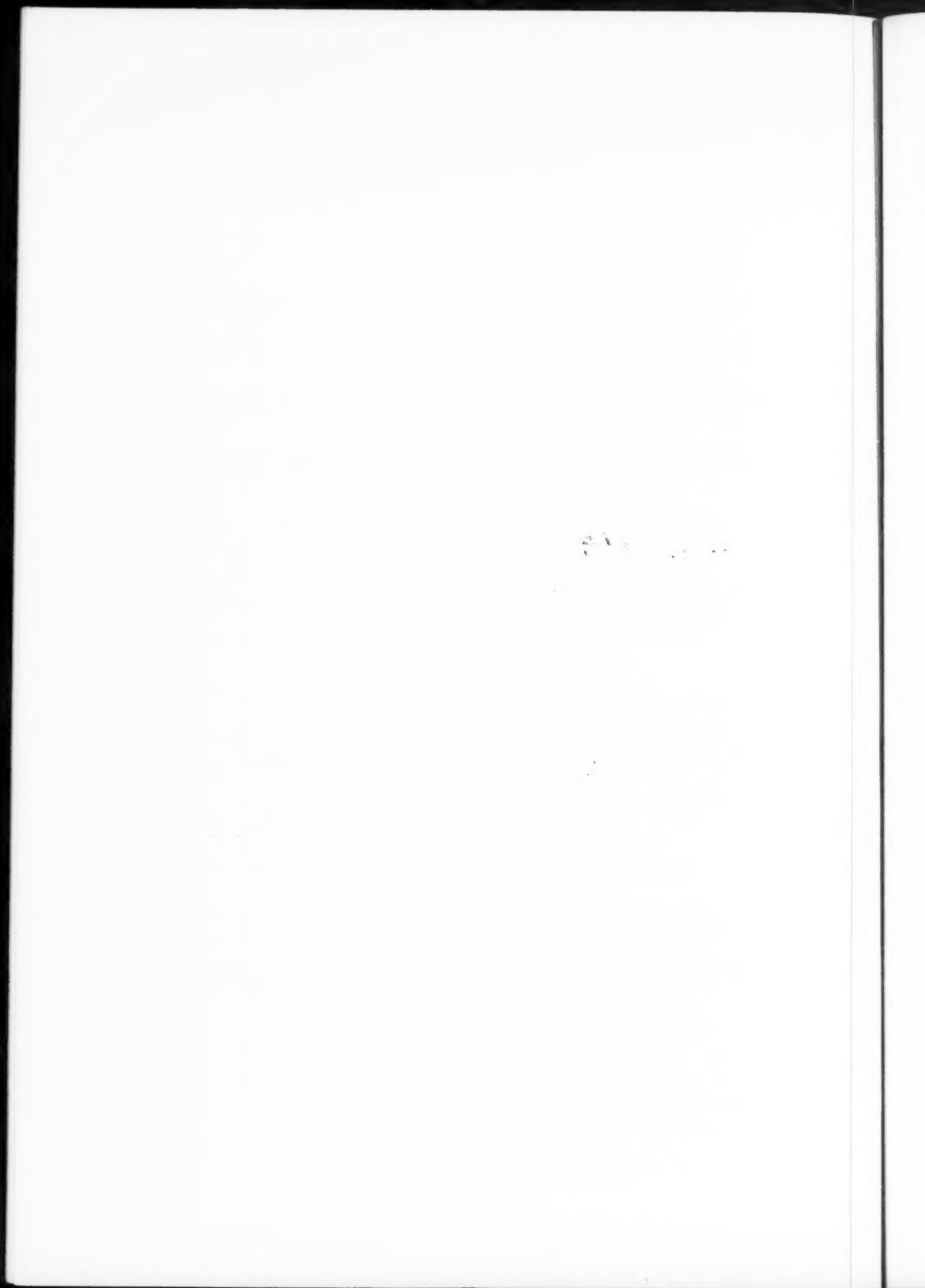


FIG. 7.—RADIOGRAM OF CASE 3 (9/9/37) SHOWING CONSOLIDATION WITH EXCAVATION OF RIGHT UPPER LOBE, AND DIFFUSE FINE MOTTLE OF THE RIGHT MIDDLE AND LOWER ZONES.  
Note the retraction upwards of the interlobar septum.





On admission the temperature was  $99.2^{\circ}$ . Examination of the chest showed dullness over the upper half on the right side in front and behind, with bronchial breathing and sticky rhonchi and fine râles. X-ray examination (Fig. 2, 23/3/37) showed that the dense opacity seen in the portable radiogram had cleared to a considerable extent, but irregular patchy mottling was visible in all zones of the right lung, especially in the upper lobe. The erythrocyte sedimentation rate was 100 mm. at the end of one hour (Westergren scale). There was very little cough, and it was difficult to obtain any sputum; a scanty specimen collected on March 30 showed no tubercle bacilli.

At the end of a fortnight her condition had improved considerably; the physical signs in the chest were less obvious; the erythrocyte sedimentation rate was now 50 (Westergren); the temperature remained at  $99^{\circ}$ . X-ray examination (Fig. 3, 13/4/37) showed an appreciable diminution in the mottling previously seen. By May 3 she appeared perfectly well; the physical signs in the chest had cleared up entirely, the temperature was normal, and the erythrocyte sedimentation rate was 9 (Westergren) at the end of an hour. X-ray examination showed that the mottling on the right side was still less obvious. She was discharged from hospital on May 9, and subsequently went to the seaside for convalescence, which was uneventful. When seen again in the autumn she was feeling very fit; no abnormal physical signs were found in the chest. X-ray examination (Fig. 4, 27/9/37) showed that the lung fields were now clear. Since then she has remained well.

CASE 2.—Mrs. M., aged thirty-five, had been feeling very tired and out of sorts for several months, and had been losing weight. In the spring of 1940 she had a bad cold and went to bed for a few days. She was then allowed up, but her cough continued to be troublesome; sputum was small in amount; no tubercle bacilli were found.

When examined by one of us (M. D.), on April 4, she had physical signs of consolidation of the left upper lobe (dullness, with bronchial breathing and bronchophony, and numerous fine râles in front and behind at the end of inspiration). The whole clinical picture was typical of phthisis, and the X-ray appearances (Fig. 5, 3/4/40) suggested extensive infiltration of the left upper lobe.

The patient was very depressed and pessimistic about the future. It was pointed out to her that the outlook was by no means hopeless, and that with complete rest under proper medical supervision there was a reasonable chance that the disease in the lung would undergo healing. She was kept in bed on strict rest, and after about two months her doctor had another radiogram of the chest which showed the appearances seen in Fig. 6 (5/6/40). It will be seen that almost complete resolution of the infiltration has occurred. The patient's cough is better, and her general condition has greatly improved.

CASE 3.—O. C., female, aged eighteen, a stencil worker, was first seen by one of us (P. E.) in September, 1937, when she complained of loss of

weight, lassitude, and anorexia. She had had a cough, without sputum, for about four months; the temperature range was  $97^{\circ}$  to  $100^{\circ}$ , the pulse rate 140. A diagnosis was made of adolescent phthisis.

There was no history of any previous illness of importance. Her father was known to be suffering from pulmonary tuberculosis.

She was admitted to a sanatorium on September 16, 1937. She was then getting profuse night sweats and was obviously ill and tired. There were definite physical signs of active disease: crepitations were audible in the upper zones of both lungs, and there was evidence of excavation of the right upper lobe. The erythrocyte sedimentation rate was 55 mm. at the end of the first hour (Westergren scale). X-ray examination (Fig. 7, 9/9/37) showed a dense consolidation of the right upper lobe with a large cavity; the opacity in this region has a sharply defined lower edge corresponding to the interlobar septum, which appears to be somewhat drawn up. There is diffuse fine mottling of the middle and lower zones of the right lung, the appearances being similar to those seen in certain cases of chronic miliary tuberculosis. In the left upper zone there are appearances of infiltration with some fibrosis; the middle and lower zones show a fine mottling similar to that seen on the right side, but less marked.

Three unsuccessful attempts were made to induce an artificial pneumothorax on the right side. The patient was put on absolute rest for three months, after which some relaxation of the strict régime was permitted, but she still remained resting in bed until May, 1938. Two courses of gold therapy were given, 6 gm. of solganol in all being administered.

Successive X-ray examinations showed a gradual clearing of the lung fields with increasing retraction of the interlobar septum on the right side. The radiogram taken in July of that year (Fig. 8, 13/7/38) still shows an obvious cavity in the right upper lobe, the sharp lower edge of the opacity being appreciably higher in position in comparison with that seen in Fig. 7. The fine diffuse mottling has entirely disappeared; the left apex is almost clear. The patient was discharged from the sanatorium on September 2, 1938, weighing 7 st. 12 lb. (her weight on admission had been 6 st. 5 lb.). She was now afebrile and free from symptoms; the pulse rate was from 90 to 100. Physical examination of the chest revealed tubular breathing in the right upper zone, with post-tussive crepitations. The next radiogram (Fig. 9, 15/8/39), nearly a year after her discharge, shows still further retraction of the fibrous tissue at the right apex, the cavity within being almost obliterated. The remainder of the lung fields is clear. The erythrocyte sedimentation rate was 12 (Westergren) at the end of an hour.

When seen again on June 6, 1940, she was feeling perfectly well and had been working at a sedentary job from 8 a.m. to 6 p.m. There was no cough or sputum; her weight was 8 st. 1 lb. Physical examination revealed dullness in the right upper zone without signs suggestive of excavation. No adventitious sounds were heard. A further radiogram taken at this date showed residual fibrosis of the right apex, with complete obliteration of the cavity. Apart from a small scar at the extreme apex of the left lung, the remainder of the lung fields appeared normal. The erythrocyte sedimentation rate was 9 mm. (Westergren) at the end of an hour.

# PLATE IV.

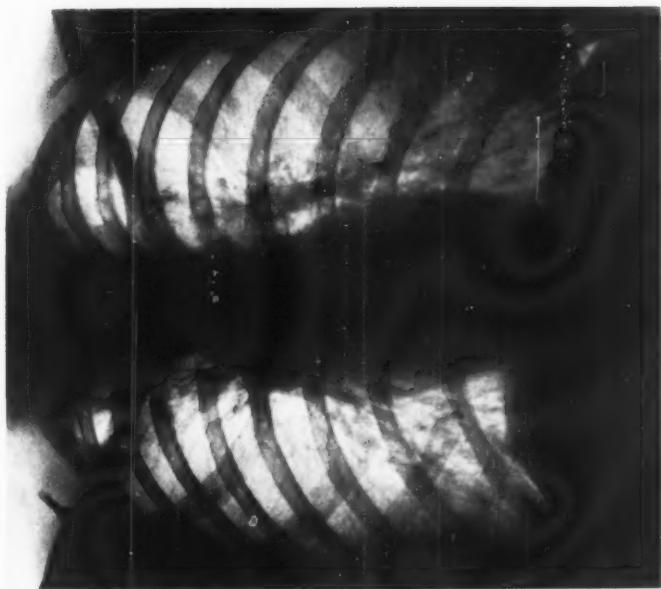


FIG. 8.—RADIOGRAM OF CASE 3 (13/7/38) SHOWING FURTHER RETRACTION OF THE INTERLOBAR SEPTUM WITH SOME DIMINUTION IN SIZE OF THE CAVITY.  
The diffuse mottling in the middle and lower zones has cleared up.

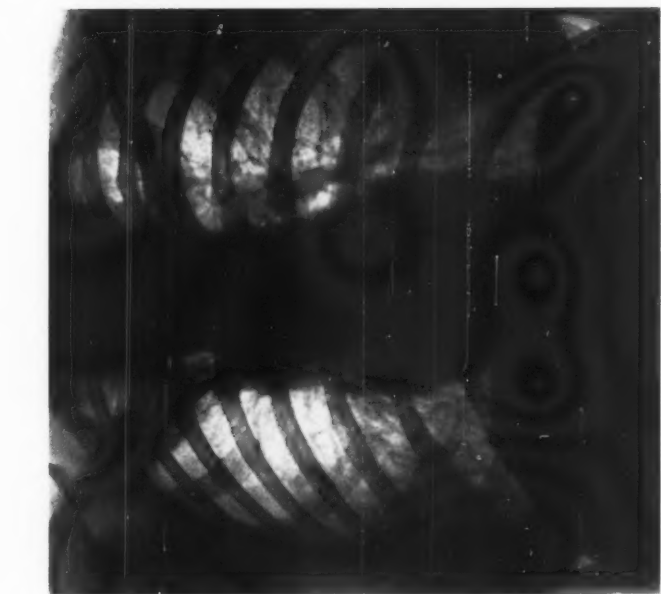


FIG. 9.—RADIOGRAM OF CASE 3 (15/8/39) SHOWING STILL FURTHER RETRACTION OF THE INTERLOBAR SEPTUM, THE CAVITY BEING NOW ALMOST OBLITERATED.

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PLATE V.

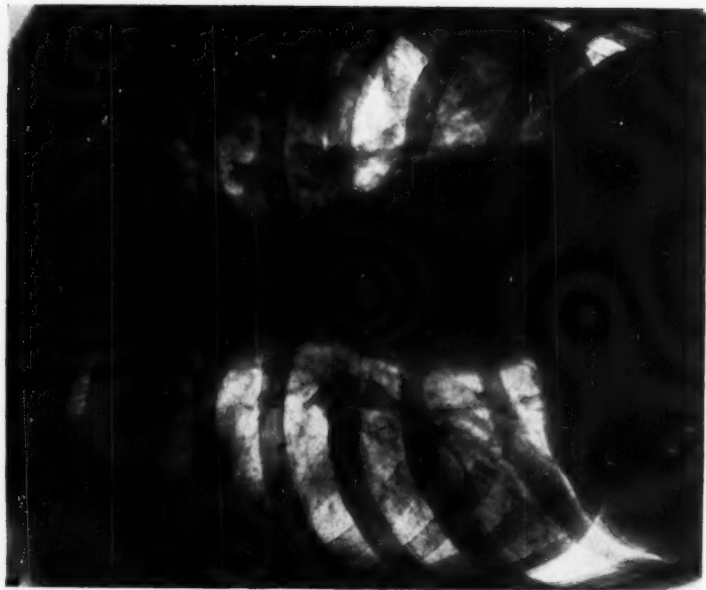


FIG. 10.—RADIOGRAM OF CASE 4 (17/7/35) SHOWING EXTENSIVE  
COARSE IRREGULAR MOTTLING OF BOTH LUNGS.  
No definite appearances of excavation are seen.

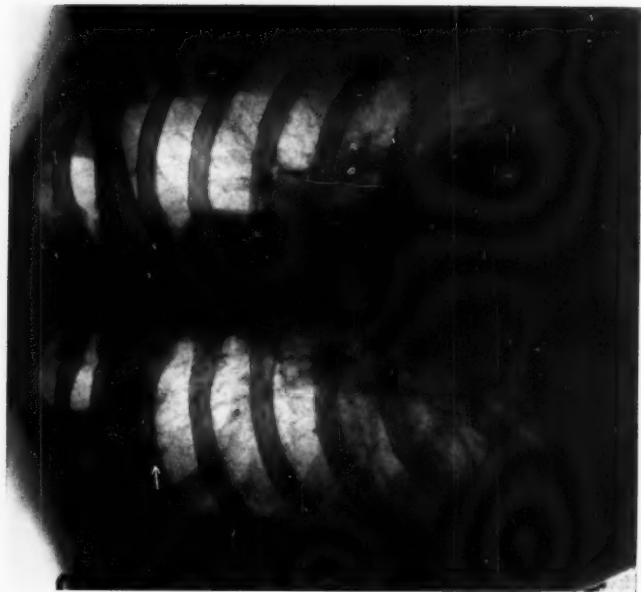


FIG. 11.—RADIOGRAM OF CASE 4 (23/5/37) SHOWING  
COMPLETE RESOLUTION.  
Note the small scar, indicated by an arrow, in the right upper zone.

CASE 4.—A. P., aged fifty, female, married, gave a history of pneumonia in childhood, left-sided pleurisy in 1934, and bronchitis in January, 1935. The family history is, perhaps, of some significance, her brother-in-law having died of pulmonary tuberculosis in 1917, her husband also having succumbed to this disease in April, 1940. For about three months prior to her husband's death she had been nursing him. He had apparently had phthisis for many years before he became an invalid, and may well have been a source of primary infection.

When first seen by one of us (P. E.) in June, 1935, she complained of a persistent hacking cough of three months' duration, without expectoration, following an attack of bronchitis at the end of January. She had lost a stone in weight in about two months, and she also complained of excessive fatigue and of night sweats. On examination she appeared ill and wasted (weight 8 st. 5 lb.), her temperature ranged from 97° to 100°, her pulse rate averaged 100, the erythrocyte sedimentation rate was 18 mm. (Westergren) at the end of one hour. The chest moved badly; there was wasting of the muscles in the left supraclavicular and infraclavicular fossæ. The percussion note at both apices was impaired, the breath sounds in the left upper zone were bronchial in character, and fine crepitations, increased after coughing, were heard at the end of inspiration over the upper zones of both lungs, especially in the supraspinous regions. Radiological examination of the chest at this stage showed restricted movements of the diaphragm. The film (Fig. 10, 17/7/35) shows coarse irregular mottling in the upper zone of the right lung field and in the upper and middle zones of the left lung field; there is nothing in the adventitious shadows definitely to suggest the occurrence of excavation. The appearances were regarded as practically identical with those characteristic of pulmonary tuberculosis. The patient was admitted to a sanatorium on September 2, 1935.

She was kept in bed at complete rest for three months, and was eventually discharged on February 22, 1936. She was then afebrile and had gained 4 lb. in weight. The physical signs in the chest had cleared up to a large extent, but she still had bronchial breathing in the left upper zone. X-ray examination at this time revealed no appreciable change. Throughout her stay in the sanatorium she had had no sputum. By May 11, 1937, her weight had dropped again to 8 st., and she had a cough with traces of sputum, in which no tubercle bacilli could be found after repeated examinations by ordinary methods, by the antiformin method, and by culture. There were now no gross abnormal physical signs, and radiological examination showed remarkable and almost incredible evidence of healing by resolution of the original lesions described above (see Fig. 11, 25/5/37). The film of this date shows an almost normal radiogram, the lung fields being clear, but below the right clavicle and crossing the fifth rib in its posterior aspect is a small linear shadow suggestive of a fibrous scar, the only remains of the original lesion. The striking improvement in the radiological picture was not accompanied by any commensurate change in the patient's general condition.

On September 6, 1937, she had an attack of influenza (*sic*). Her weight had now dropped to 7 st. 6 lb.; she had a cough with slight muco-purulent

sputum (which still showed no tubercle bacilli present), and she had marked symptoms of general malaise, though there was little febrile reaction. There were slight physical signs of disease at the left apex, and radiological examination (Fig. 12, 28/9/37) now showed a recurrence of the infiltration, which, however, though bilateral, appeared to be more localised than at the first examination in 1935 (*cf.* Fig. 10).

On February 14, 1938, after a prolonged period of rest, her weight had returned to 8 st. Cough persisted, with slight muco-purulent sputum (still negative for tubercle bacilli); no abnormal physical signs were to be found in the chest, and X-ray examination (Fig. 13, 15/2/38) again showed resolution of the infiltration, the appearances having reverted to those seen in Fig. 11.

In the early autumn of 1938 she had an acute respiratory infection (so-called influenza), which was accompanied by a third slight recurrence of infiltration, again indicated in a radiogram of September 20. This in turn exhibited a retrogression similar to the previous two, but in a final radiogram of May 1, 1940, the lung fields were perfectly clear, the linear scar in the right upper zone being faintly visible, as in Figs. 11 and 13.

Up to the time of writing she has kept free from abnormal physical signs, and sputum examinations by all methods have failed to show the presence of tubercle bacilli.

CASE 5.—K. O., female, aged thirty-five, married, was admitted to one of the large municipal hospitals on May 5, 1940, with a history of having had a so-called influenzal attack succeeded by bronchitis; she had developed a sudden pain in the chest, and in view of the clinical picture which was then presented a provisional diagnosis of broncho-pneumonia was made. M. and B. 693 was given for six days, after which the temperature, which had been high, began to fall. X-ray examination on May 16 (Fig. 14) showed a coarsely mottled opacity in the left upper and middle zones, indicative of a large area of inflammation in the lung parenchyma; the appearances were then thought to indicate either a lung abscess or pulmonary tuberculosis. The next radiogram (May 29, Fig. 15) showed the same large area of diffuse pneumonitis, in the upper part of which, however, a large cavity was visible, the size of a half-crown, and having a definite fluid level. On June 28 a radiogram showed considerable resolution of the general inflammatory reaction; the large cavity observed in the previous film was no longer seen, but numerous much smaller cavities were now visible. A further radiogram on July 15 (Fig. 16) showed still more clearing of the general opacity; in the upper zone, about two inches below the clavicle, was seen a thin-walled cavity about the size of a shilling, corresponding in position approximately to that shown in the first film of May 29. The radiological picture at this period is, in our view, indistinguishable from that of a patient with tuberculous infiltration and fibrosis of the left upper zone, with a typical thin-walled cavity near the apex. On August 1 the X-ray appearances were similar to those of July 15, but indicated further resolution, the shadows being somewhat harder in character, and the apical cavity being much smaller (about half the size). On August 14 the cavity was only just visible, and on August 27 almost all traces of excavation had disappeared, the X-ray



PLATE VI.

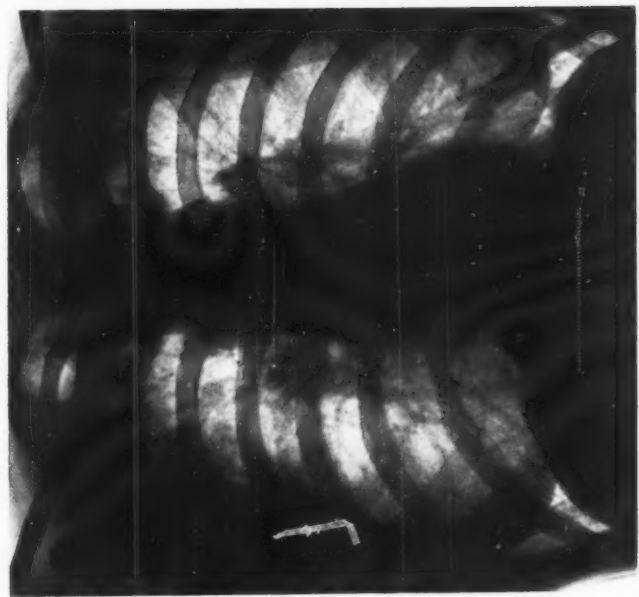


FIG. 12.—RADIOGRAM OF CASE 4 (29/9/37) SHOWING REAPPEARANCE OF DISEASE IN BOTH UPPER ZONES.  
The infiltration appears more localized than that seen in Fig. 10.

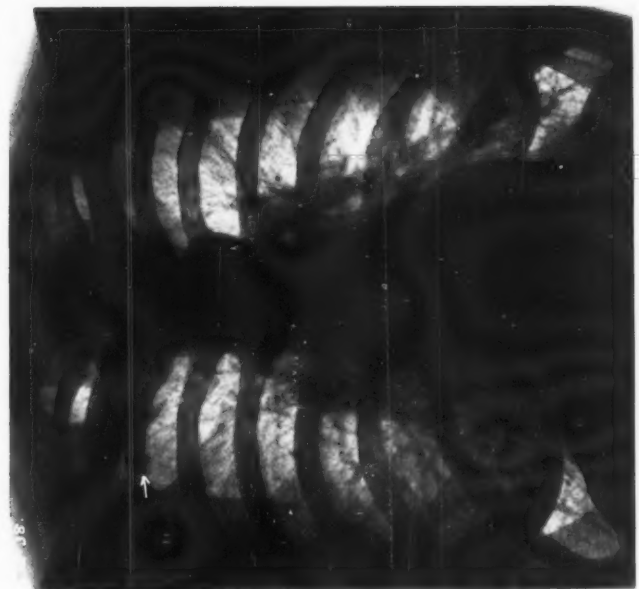


FIG. 13.—RADIOGRAM OF CASE 4 (15/2/38) SHOWING RESOLUTION OF DISEASE FOR THE SECOND TIME.  
The scar in the right upper zone, indicated by an arrow, is again visible.

[To face page 10.

PLATE VII.



16.5. '40.

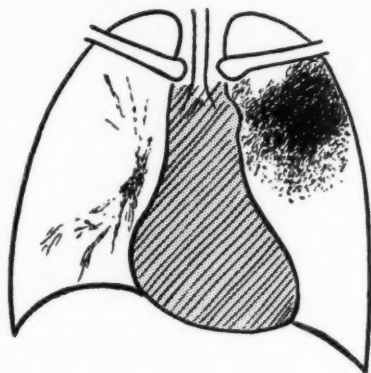


FIG. 14.—RADIOGRAM OF CASE 5 (16/5/40) SHOWING A LARGE AREA OF CONSOLIDATION IN THE LEFT UPPER AND MIDDLE ZONES.  
No definite excavation can be seen.

PLATE VIII.



29·5·'40.

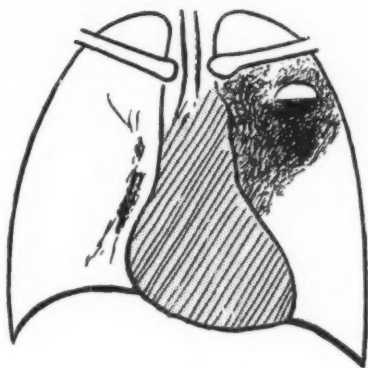
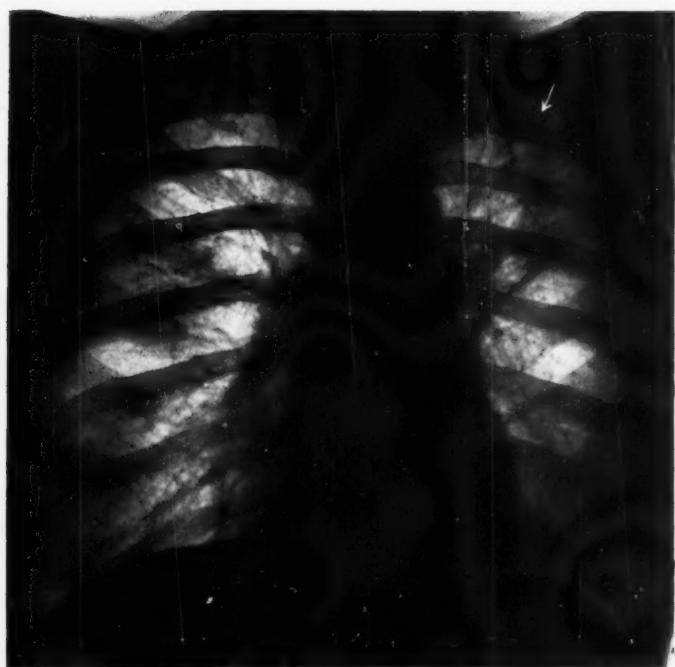


FIG. 15.—RADIOGRAM OF CASE 5 (29/5/40) SHOWING THE SAME  
OPACITY AS IN FIG. 14.

A definite cavity, with a fluid level, is now visible within the  
area of consolidation.

PLATE IX.



15.7.'40.

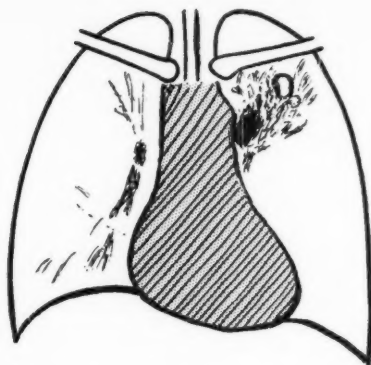
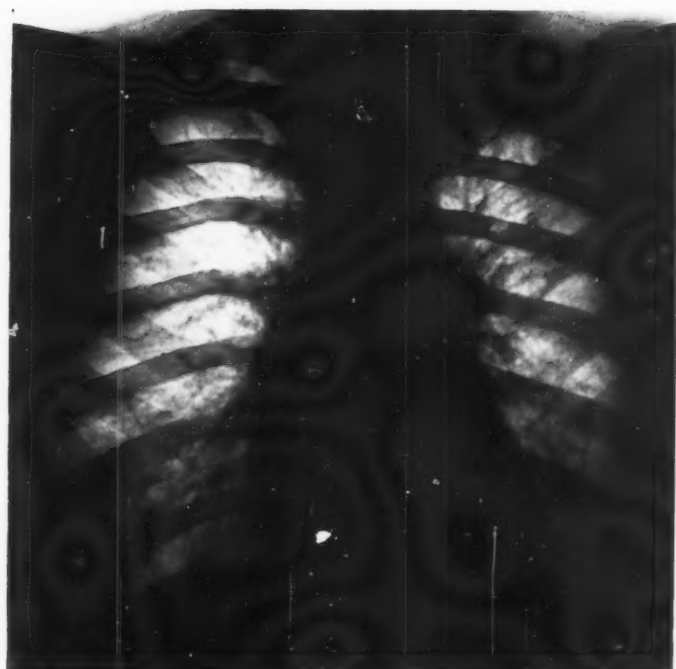


FIG. 16.—RADIOGRAM OF CASE 5 (15/7/40) SHOWING CONSIDERABLE CLEARING OF THE GENERAL OPACITY SEEN IN FIGS. 14 AND 15.

A thin-walled cavity is visible in the left upper zone, below the inner end of the clavicle.

PLATE X.



27.8.'40.

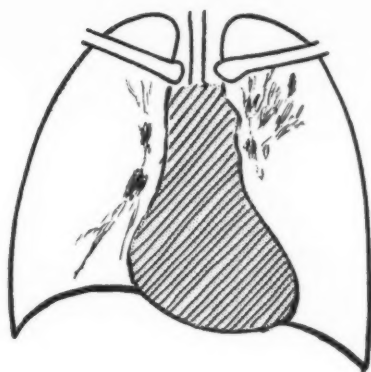
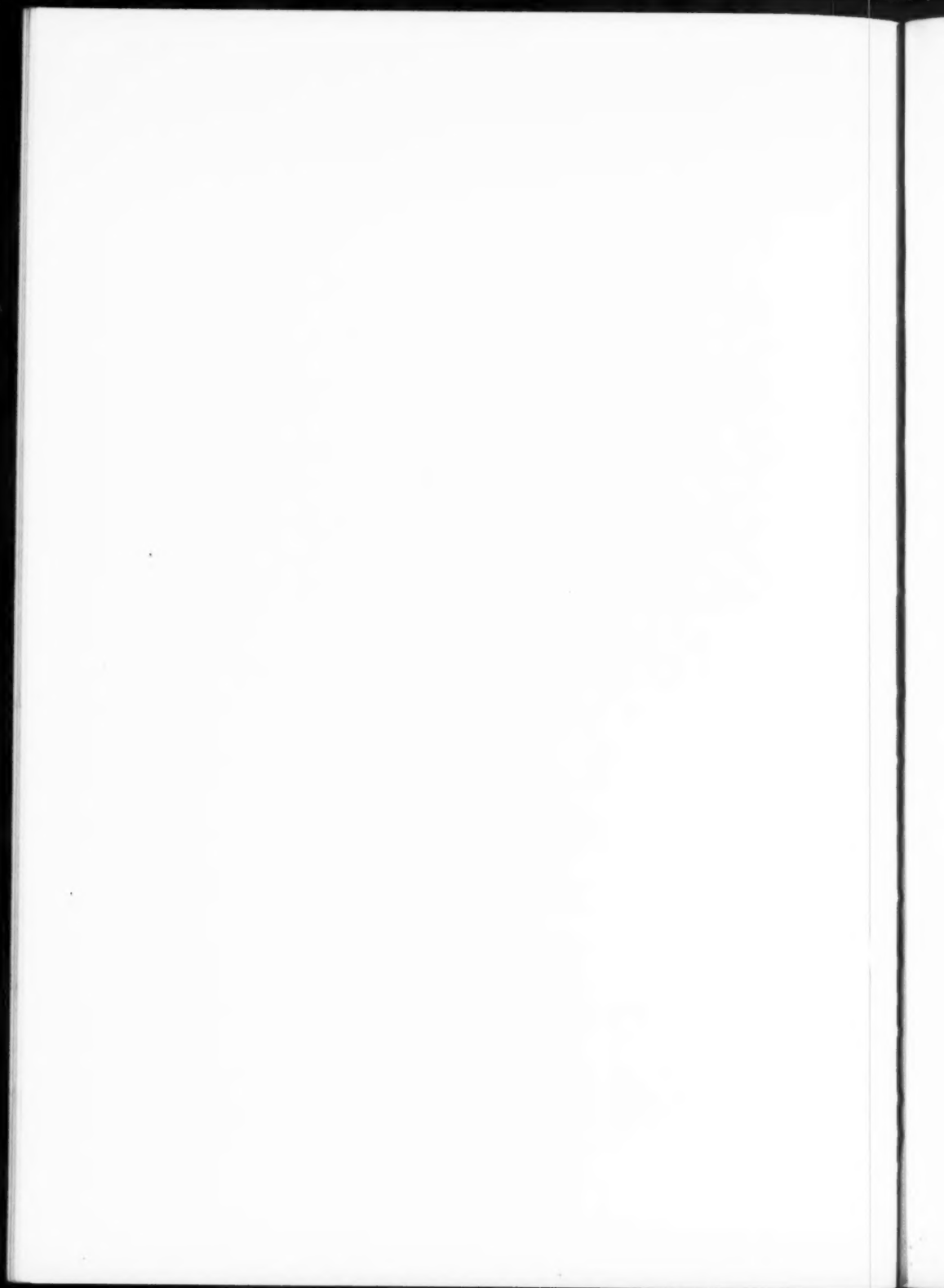


FIG. 17.—RADIOGRAM OF CASE 5 (27/8/40) SHOWING STILL FURTHER RESOLUTION OF DISEASE, WITH RESIDUAL FIBROSIS IN THE LEFT UPPER ZONE.

The cavity has now practically disappeared.



appearances (Fig. 17) indicating only scarring of the left upper and middle zones from residual fibrosis. The picture now was typical of an old arrested and partly healed tuberculous lesion.

The clinical history of this case is interesting. The patient had suffered from attacks of bronchitis regularly every winter, and for the past five years had spent three or four weeks in hospital every winter by reason of this. At the age of twenty-two she had had a hæmoptysis (alleged to have followed a strain), and on two occasions had brought up a cupful of blood. Her father had died of asthma and bronchitis, her mother had died from tuberculosis. She had three children, aged fourteen, eight, and five respectively, all healthy. For administrative reasons she was evacuated from the municipal hospital in London to another institution some miles out of town, where she came under the observation of one of us (P. E.) on July 12. By this time her general condition, which at the onset of this illness had been serious, had greatly improved. For a few days she had very slight irregular fever (the temperature not rising above 99°), after which she remained afebrile. There was slight enlargement of the cervical glands. Beyond some impairment of the percussion note in the left upper zone, with some diminution of the respiratory murmur, there were no physical signs of importance in the chest. There was no clubbing of the fingers. Examination of the sputum, which was mucoid, showed the presence of *M. catarrhalis* and some pneumococci, but repeated examinations for tubercle bacilli by all methods, including gastric lavage, gave negative results. The following blood examinations are of interest.

July 27.

Total leucocyte count. 14,400 per c.mm.

Differential count.	Polymorphonuclears	64 per cent.
	Lymphocytes	30.8 per cent.
	Eosinophiles	5.2 per cent.

Erythrocyte sedimentation rate.	19 mm. (Westergren) after 1 hour.
	32 mm.                   "                   "   2 hours.

August 1.

Erythrocyte sedimentation rate.	12 mm. (Westergren) after 1 hour.
	23 mm.                   "                   "   2 hours.

August 12.

Erythrocyte sedimentation rate.	11 mm. (Westergren) after 1 hour.
	21 mm.                   "                   "   2 hours.

### Discussion

*Review of Case Reports in Relation to Contemporary Literature.*—The differences in the clinical and radiological pictures in these five cases are considerable; one feature common to all of them is the absence of tubercle bacilli in the sputum. In the first two the sputum was scanty, the result of bacteriological examination for tubercle bacilli by ordinary methods being negative. In Case 3 the patient was sputum-free throughout her illness. In Cases 4 and 5



repeated examinations of sputum by all methods at frequent intervals failed to show the presence of tubercle bacilli. In spite of the absence of bacteriological proof, we are still prepared to regard all five cases as manifestations, in different forms, of pulmonary tuberculosis. Clinically and radiologically there is most resemblance between Cases 1 and 2, which differ mainly in the length of the clinical history. It is of interest to consider these two a little further in the light of some of the literature of the last decade.

In 1931 Ornstein, Ulmar, and Dittler<sup>16</sup> published some extremely valuable observations on a series of 58 cases described as "benign acute pulmonary tuberculosis". Most of their patients were young adults, the course of events in the average case being as follows: After a period of perfect health, a slight cough developed which usually cleared up within a week; expectoration was scanty and continued only for a few days, so that if tubercle bacilli were to be found they had to be sought within a few days of onset of illness. Apart from a little impairment of resonance, some diminution in the intensity of the respiratory murmur, and the occasional presence of a few fine râles, which persisted for varying periods, the physical signs were not prominent and gave little information in comparison with that afforded by a radiogram, which showed a fairly dense homogeneous opacity, often involving an entire upper lobe and showing a sharp lower border corresponding to the interlobar fissure. The subsequent course of these cases was characterised by a rapid resolution of the inflammatory reaction in the lung, the physical signs and the radiological opacity clearing up within a remarkably short period, sometimes as little as three weeks. The authors describe two main ways in which the radiographic shadow tends to disappear. In the first there is a uniform diminution of density; in the second, the more usual, there is an irregular absorption of the opacity, which at a certain stage gives rise to a patchy mottling. Occasionally complete absorption appears in the centre of the shadow, so that a picture is seen which suggests the presence of a large cavity. The appearances not infrequently bear a strong resemblance to those seen in ordinary pulmonary tuberculosis of the chronic proliferative type, from which in fact they may be practically indistinguishable. The ultimate radiographic picture shows (within a period varying from six weeks to a few months) a complete disappearance of all pathological shadows.

We have referred to these observations at some length since they describe objective phenomena of disease which correspond so closely to those of Case 1 in our own series, which case seems to us to fall into the same group and for which we feel that a diagnosis of benign acute pulmonary tuberculosis is justified; it seems indeed difficult to place it in any other category.

Three points especially are of importance in the American records.

Out of the 58 patients 25 (*i.e.*, 43.1 per cent.) were sputum positive, and all of these had an acute onset. In 22 per cent. there was a definite history of exposure to tuberculosis. Hæmoptysis, often an initial symptom, occurred in 43 per cent.

Case 1 in our series shows a clinical history closely resembling that described by these authors, and the X-ray appearances (Fig. 2) illustrate the patchy mottling which marks the earlier stage of commencing resolution. In this instance a portable X-ray examination, made some days earlier, showed evidence of consolidation, the opacity being more homogeneous in character. A similar case was reported by one of us (M. D.)<sup>5</sup> in 1935, in which lobar consolidation was seen in the first radiogram, the patchy mottling being just apparent through the general opacity, complete resolution being seen sixteen days later in a second X-ray film.

Case 2 is similar to Case 1 from the radiological standpoint, but here the clinical history was of longer duration and conformed much more to the typical story usually obtained in chronic phthisis. In this instance X-ray evidence of complete resolution was seen at the end of two months. This, in view of the clinical picture, was somewhat unexpected, no suspicion having been entertained, in spite of the negative bacteriological findings, that the case was anything but one of ordinary chronic pulmonary tuberculosis with characteristic physical signs and a typical history of gradually progressive general toxæmia. Although we are strongly inclined to classify these two examples, Case 1 in particular, with those of the American authors just quoted, and to accept their view of the pathogenesis of this benign type of tuberculous infection (*viz.*, that it represents the reaction to a minute dose of tubercle bacilli of a person with a low threshold level—*i.e.*, with a high degree of allergy), there are other suggestions which may be advanced and which must be taken into account.

In the first place we have to think of the possibility of a non-tuberculous inflammatory reaction in the lung and to consider the numerous instances of non-tuberculous pulmonary inflammations cited by Scadding and others under the headings of pneumonitis, atypical pneumonia, etc. Of these Scadding's disseminated focal pneumonia, described by him in 1937, approaches most nearly to the type we are discussing. In his paper<sup>22</sup> he notes the resemblance of the radiological changes to those of pulmonary tuberculosis in four selected cases which appeared to form a recognisable clinico-radiological group and in which the bacteriological features were determined with considerable care and accuracy, *Strep. viridans* being a constant finding, and tubercle bacilli being conspicuous by their absence. This last point is, of course, a strong argument in the hands of those who refuse to accept the explanation of Ornstein and his colleagues, and it

receives further corroboration from the autopsy findings in three other cases reported by Scadding<sup>20</sup> in 1936, which demonstrated a pneumonia, in diffuse foci, showing recent consolidation, resolution, organisation, and suppuration. The term "disseminated focal pneumonia" was adopted by Scadding not only as a convenient term clinically, but also as one which involved no aetiological assumptions. In discussing the differential diagnosis he lays stress on two points: first, the absence in focal pneumonia of the relation between fever and exertion which usually characterises tuberculosis; second, the relatively sudden increase in the amount of purulent sputum, which, he points out, would hardly be expected in pulmonary tuberculosis unless gross excavation had occurred.

The lung changes occurring in association with influenza reported by Scadding<sup>21</sup> in 1937 and the atypical pneumonia described two years later by Rainey and Burbidge<sup>17</sup> may possibly have some bearing on this question, but in these cases, while in some respects they resembled our own, the pulmonary lesions were more frequently basal, and the onset of the illness was associated with the prevalence of epidemics.

Similar pictures are again shown in a recent paper by Ramsay and Scadding,<sup>18</sup> in which certain broncho-pulmonary inflammations, associated with transient radiographic shadows, are described by the authors as benign in character, though they do not commit themselves to any final view as to their aetiology.

In support of the contention that such clinical and radiological phenomena may be manifestations of tuberculosis we would draw attention to the references in recent literature to examples of the so-called "progressive primary tuberculous complex". Louria<sup>13</sup> gives details of two striking instances of this, in which the evidence of tuberculous infection is strong in the one and conclusive in the other. In the first, a girl of fourteen belonging to the white race, there was a history of malaise for ten days, fever of a week's duration, and slight unproductive cough. There was no previous medical history of importance. The only abnormal physical sign was slight impairment of resonance on the right side of the chest below the angle of the scapula. A rash was seen on the legs, consisting of about a dozen scattered papules, about 1 cm. in diameter, somewhat tender on pressure, and bearing some resemblance to erythema nodosum, from which, however, it differed in certain particulars. A tuberculin (patch) test was strongly positive. X-ray examination showed a large hilar opacity on the right side, apparently due to enlarged and inflamed tracheo-bronchial glands, with a shadow at the right base which was thought to be an inflammatory reaction in the lung parenchyma. Later radiograms showed a marked decrease of the peri-hilar adenopathy and a clearing up of the area of infiltration in

the right lower zone. The author cites this as an instance of a primary tuberculous complex which, instead of remaining asymptomatic and healing as usual without event, progressed and gave rise to obvious clinical manifestations. In support of this view he cites a second case, a coloured girl aged fifteen who, after malaise, fever, and intermittent cough of a few weeks' duration, developed a blood-stained pleural effusion on the right side. At first, attempts to find tubercle bacilli by sputum examination, gastric lavage, etc., were unavailing, but after two months one positive sputum was obtained. When the patient eventually died owing to recurrent pericardial effusions autopsy revealed a large area of consolidation in the right lower lobe with central caseation. Numerous caseating tracheo-bronchial and mesenteric glands were found, as well as tubercles and areas of ulceration in the ileum.

Although in Louria's cases just quoted there is no statement as to whether the tuberculin reaction had been obtained before the onset of manifest illness, examples are to be found in which transition from a negative to a positive reaction has been accompanied by clinical and radiological phenomena similar to those just described. So far as we are aware no observations are on record in regard to the Mantoux reaction in cases described as benign acute pulmonary tuberculosis.

Many other authors have discussed this aspect of the pathogenesis of pulmonary tuberculosis in the adult; a consideration of some recent publications is important in connection with the diagnosis of pulmonary infections of uncertain origin.

Sweany<sup>25</sup> speaks of the overwhelming primary infection of adults, where "the whole process is waged in the parenchyma as a pneumonic or ulcerative process, just as described for children", and points out that many of these cases have no resemblance to primary lesions as ordinarily seen, few of them, in fact, showing even a remnant of the primary complex. He divides them into two groups—viz., those which are fatal within a short time, and those which recover, for the time being at least. Sometimes recovery may be complete, although the initial phases of the disease often present all the intense and violent symptoms of the fatal cases. Such cases he regards as possibly analogous to Ornstein's benign acute tuberculosis.

Malmros and Hedvall,<sup>14</sup> commenting on the apparent increase noted by various Scandinavian and American workers in the number of persons who reach adult life without becoming tuberculin-positive, have recorded some extremely important observations on the incidence and significance of primary infection in such adults. Altogether they examined 3,336 students and probationer nurses, and found that, out of this total, 604 (*i.e.*, about 18 per cent.) did not react to tuberculin. No less than 151 of these negative

reactors subsequently became positive during the period of observation. In 104 of these cases no manifest symptoms occurred, but in the remaining 47 tuberculous changes were noted, either immediately, in association with the primary infection, or some time later. The individuals who exhibited such manifest clinical changes were especially associated with regular exposure to tuberculous infection. The manifestations included erythema nodosum, phlyctena, adenitis, pleurisy, miliary tuberculosis, and pulmonary tuberculosis. In 26 out of the 47 cases no primary complex could be shown. It is interesting to note that in the first developmental stage of pulmonary tuberculosis with "initial lesions" in the apical or subclavicular regions, which these authors observed in 19 cases, there were seldom any subjective symptoms of disease, the erythrocyte sedimentation rate being normal. In the few cases in which symptoms did occur, they simulated those of influenza; in some instances the occurrence of cough, fatigue, fever or hæmoptysis was observed. Often the disease proved to be progressive and malignant in type.

Schwartz and Auerbach,<sup>24</sup> in a review of 1,286 autopsies at the Sea View Hospital, observed that out of this total 32 were cases which had been sent to hospital ostensibly as cases of advanced pulmonary tuberculosis, but which proved to be examples of non-tuberculous pulmonary disease without any evidence of pulmonary tuberculosis. Of these 32 cases, 17 were lung carcinomata, 5 were lung abscesses, 5 were pneumonokonioses, 3 were bronchiectasis, and 2 were actinomycosis. Among the many interesting radiograms reproduced in this paper are two examples of carcinoma of the lung in which the appearances are practically indistinguishable from those of chronic pulmonary tuberculosis (productive type of lesions). Similar cases are quoted and illustrated by Freedlander and Wolpaw.<sup>7</sup> Schwartz and Auerbach emphasise the important point that, in the absence of pathognomonic bacteriological proof of pulmonary tuberculosis, X-ray examination, though furnishing the most accurate means of detecting this disease, *is by no means infallible* (our italics). They remind us that lobar consolidation may be caused by tuberculosis, by pneumonia, by cancer, or by abscess, and that excavation of the lung may be due to tuberculosis, abscess, cancer, gangrene, or bronchiectasis; also that fibrosis and nodulation may be produced by tuberculosis, by silicosis, or by residua of non-specific pulmonary infection, and that miliary deposits may be caused by tuberculosis, by carcinoma, by broncho-pneumonia, or by the pneumonokonioses. "There is no roentgen picture", they conclude, "that cannot be produced by both pulmonary tuberculosis and a non-tuberculous disease. Serial roentgenography is of much more value than a single film. History and physical examination cannot be relied upon alone to make final diagnoses.



Physical findings notoriously may be insignificant or even misleading in pulmonary disease." Bronchoscopy, as Myerson<sup>15</sup> has shown in numerous cases, may be of diagnostic value in tuberculosis of the respiratory tract.

An interesting and valuable summary of research on the question of primary tuberculous infection in adult life is contained in the supplement to the *American Review of Tuberculosis*.<sup>26</sup>

The lobar localisation of phthisis was emphasised as long ago as 1916 by Rist, who in a more recent communication<sup>19</sup> maintained that "the first stage of pulmonary tuberculosis in the adult is *always made up of a pneumonic attack* [our italics], the lesion being rather extended from the beginning and showing a very early tendency to localisation". He goes on to say, "the initial pneumonic lesion may eventually be totally absorbed in some rather exceptional instances".

It is difficult to sum up the different views which have been expressed on this subject with any dogmatic conclusion in regard to the ætiology of acute or subacute pulmonary inflammations of this type. The suggestion of Kayne, Pagel, and O'Shaughnessy<sup>11</sup> in regard to the observations of Ornstein and his colleagues on benign acute pulmonary tuberculosis is interesting and on the whole reflects to some extent our own view of the matter. They say (*loc. cit.*): "We feel that the authors have included in this group epituberculosis, true early infiltrations that clear up quickly, and probably also conditions of the type of disseminated focal pneumonia recently described by Scadding (1937)."

In comparison with the first two patients, Cases 3 and 4 present a clinical picture which is somewhat different. In both the onset was gradual, and in both there was a definite history of contact with pulmonary tuberculosis. The clinical and radiological findings in Case 3 are such as hardly admit of any doubt as to the ætiology. The diffuse spread of disease in the middle and lower zones of the right lung may be presumed to have taken place, in all probability, by way of the blood stream; the character of the shadows seen in Fig. 7 is strongly in favour of this. It is surprising, in view of the size of the cavity in the right upper lobe, that this patient had no expectoration; evidently the cavity was at no time in communication with the bronchioles, and must have been encapsulated by fibrous tissue. That a considerable degree of fibrosis had occurred may be inferred from the position of the interlobar septum.

The process of healing by resolution in pulmonary tuberculosis is a well-recognised phenomenon which was emphasised many years ago by Jaquero of Leysin.<sup>9, 10</sup> In a recent publication<sup>6</sup> by one of us (P. E.) examples were given of five cases, in four of which tubercle bacilli had been demonstrated in the sputum in considerable numbers, the fifth being sputum-negative.

In three of the cases there was obvious excavation, though no gross evidence of fibrosis was present. In all these healing took place after routine treatment with rest, the cavities being completely obliterated, but little fibrosis being apparent in the final radiograms. Case 3 of the present paper is one of the most striking examples of natural healing with obliteration of a cavity with which we are familiar. As Hebert<sup>8</sup> has pointed out, neither density nor thickness of the wall of a round cavity can in itself be regarded as evidence of fibrosis, but in this instance the presence of fibrous tissue may reasonably be deduced from the drawing up of the interlobar septum shown in Fig. 7, and the further progressive retraction evident from the two succeeding radiograms (Figs. 8 and 9). Our main object in including this case in our series, apart from its intrinsic interest as an instance of healing by natural processes without the aid of collapse therapy, is to call attention to the inferential proof of the tuberculous nature of the disease afforded by the radiogram in the absence of bacteriological evidence. To some extent this may be acceptable as supporting our contention as to the tuberculous nature of the other three cases.

Case 4 is the most unusual of our series, and may almost be regarded as unique. The radiological appearance of secondary lesions in pulmonary tuberculosis, without any corresponding clinical evidence of their presence, has been emphasised by Wingfield,<sup>27, 28</sup> who has demonstrated time and again the cardinal importance of rest in their treatment. The retrogression of these secondary lesions as the result of the imposition of absolute rest is now generally acknowledged. The alternation of retrogression with progression (pendulum lung) is, however, less familiar. The frequent repetition of this phenomenon in a patient exhibiting the extent of disease evident in Case 4, with such complete ultimate resolution, is, in our experience, a most unusual event.

Of the aetiology of this case it is, of course, impossible in the absence of post-mortem evidence to speak with precision, though our own view is that the condition is tuberculous. That persistence of negative sputum, as in this instance, does not in itself necessarily exclude a diagnosis of chronic pulmonary tuberculosis can hardly be denied. There was some difference of opinion among the radiologists who viewed these films as to whether they were diagnostic of phthisis. The appearances seen in Fig. 10, if not absolutely characteristic, are certainly suggestive of tuberculosis, and by many would be regarded as indistinguishable from those of numerous proved sputum-positive cases. One of our radiological colleagues, whose experience of chest work is very extensive, regards it as unlikely that tuberculous infiltration of the extent such as is here shown would clear up so completely. Scadding in a personal communication has suggested that since this patient



had principally constitutional symptoms at the times at which the pulmonary infiltration was evident, and since catarrhal symptoms were never prominent, and moreover resolution required five months for completion, the phenomena are in favour of the diagnosis of an unusually benign tuberculous lesion. He admits that he has not seen a chronic pneumonic condition that presented these characteristics.

Case 5 is of interest chiefly in comparison with Case 4, especially from the radiological standpoint. The first radiograms showed similar appearances in both patients—*i.e.*, an extensive opacity in which a coarse mottling could be discerned, though no definite excavation was visible. Whereas in Case 4 resolution occurred without the appearance of a cavity at any time, in Case 5 resolution was noted within a shorter period, an obvious cavity being visible in the intermediate stages. While in both cases a radiological diagnosis of pulmonary tuberculosis was suggested in the first instance, in Case 4 the possibility of a non-tuberculous condition was always under discussion. In Case 5, on the other hand, the radiogram of July 15 (Fig. 16) presented a picture such as could hardly be given by any disease other than fibro-caseous phthisis, the diagnosis of which from a radiological standpoint is not likely to be disputed, in spite of the failure to show, by every possible method, the presence of tubercle bacilli.

*Differential Diagnosis.*—We referred in our introductory paragraph to the limitations of radiographic diagnosis, the problems of which may, we hope, have been rendered somewhat clearer by the foregoing discussion. In conclusion we can only repeat that the differential diagnosis between some of the less stereotyped forms of pulmonary tuberculosis and the various non-specific inflammations of the lung which may simulate these is frequently a matter of considerable difficulty. The question is not to be solved by any definite rules, and there are bound to be cases in which doubt will exist and the diagnosis remain a matter of individual opinion. Certain general considerations, however, seem to us to be permissible.

The healing of exudative tuberculous lesions of the lung parenchyma, by a process of resolution comparable to that seen in non-tuberculous pneumonic infiltrations, is a phenomenon well established by numerous clinical and radiological observations. As a rule it may be said that the length of time required for such resolution is greater in the tuberculous than in the non-tuberculous inflammations, and this must be given due consideration in arriving at a decision as to the nature of the lesion. At the same time the possibility of an underlying tuberculosis cannot be ruled out even in those cases in which resolution of a diffuse inflammatory area of lung takes place within a dramatically short period. The observations of Ornstein and others have done much to throw light upon this class of case, and to

show that the absence of bacteriological proof of tuberculosis is in many instances due to failure to recognise the benign type of pulmonary tuberculosis and to search for the tubercle bacillus in the only period in which it is likely to be discovered in this condition—*i.e.*, during the first few days of the illness. It may be added that the knowledge that natural resolution is a recognised method of healing in pulmonary tuberculosis has an extremely important bearing on the question of treatment; valuable and necessary as it may be in certain cases to initiate adequate collapse therapy at an early stage, the possibility of spontaneous healing must never be ignored, and the decision to induce an artificial pneumothorax should therefore never be precipitate.

A word must be said as to some possible explanations of natural resolution. Amberson<sup>1</sup> and others regard many of these recent lesions which show a tendency to resolution as being perifocal exudates around a central tuberculous lesion, in which comparatively few giant-cell systems and even fewer tubercle bacilli are found. Such fresh exudates seem to occur more especially in adolescence and early adult life, and tend on the whole to give rise to general constitutional disturbance rather than to local symptoms.

Another point of importance is the part which pulmonary collapse, local or general, may play in the determination of the radiographic appearances in various pulmonary inflammations. Andrus<sup>2</sup> has emphasised this in an attempt to classify into definite groups the different "shadow-complexes" seen in various cases of chronic non-specific pulmonary disease. He points out that shrinkage in lung volume may be due to acquired airlessness of the lung. "A relative increase in density and wooliness of the shadows of the pulmonary markings often results in the partly collapsed lung, which the uninitiated are apt to interpret as increase in disease. To the 'atelectasis conscious' the identification of this is simple. In acute collapse it consists of a homogeneously high opacity over the area concerned. Shrinkage in volume is identified by inward displacement of a sharply defined free margin and by gross to moderate retraction of adjacent organs. Atelectasis, however, may be patchy in distribution. In this case the local shadows are not to be distinguished from those of patchy broncho-pneumonia (with which they are in all probability usually combined)." So far as the factor of collapse is concerned, whatever may be the ætiology of the pulmonary infection, it must be remembered that pulmonary tuberculosis is no exception.

The family history may be of some significance, and should, of course, be taken into account to some extent in assessing these doubtful cases. This has reference more especially to the question of possible exposure to infection, such as was noted by Malmros and Hedvall (*loc. cit.*). In Cases 3

and 4 of our series there was a definite history of phthisis in a near relation, and these patients may well have been contacts. The occurrence of a definite hæmoptysis prior to or in the early stage of the illness, though not pathognomonic, is, in our view, strongly suggestive of the tuberculous character of the disease.

### Summary

Five cases of a subacute pulmonary infection are described in which the clinical and radiological features differ, but in which there is one common feature—viz., the persistent absence of tubercle bacilli in the sputum. It is nevertheless maintained that these may be regarded as manifestations of atypical pulmonary tuberculosis.

These subacute pulmonary affections are discussed in relation to the so-called benign acute pulmonary tuberculosis, to the progressive primary tuberculous complex, and also to disseminated focal pneumonia and other non-tuberculous broncho-pulmonary infections.

Much confusion exists as to the ætiology of these infections. Some observers have classified them as non-tuberculous, because of transient radiographic shadows and clinical and radiological evidence of healing by natural resolution. This process, however, may be common to each clinico-radiological group.

Although recent work shows that much has still to be learned about acute, subacute, and chronic inflammatory processes in the lung, and although both clinical and radiological diagnosis have undoubted limitations, it is suggested that the diagnosis of pulmonary tuberculosis is aided in such cases as these by a synthesis of the following data:

1. A family history of pulmonary tuberculosis.
2. The occurrence of constitutional symptoms in the presence of pulmonary infiltration.
3. The comparative absence of catarrhal symptoms, which are as a rule not so prominent in pulmonary tuberculosis.
4. A relatively lengthy period of resolution.
5. The relation of pyrexia to physical exertion, prominent in tuberculosis, and the more definite response of the latter to absolute rest.

It must also be recognised that there exists an infiltration of lung tissue which gives rise to radiological shadows almost identical with those of pulmonary tuberculosis, but which are not, apparently, connected with the tubercle bacillus.

Our acknowledgments and thanks are due to Dr. Louise Livingstone for her kind permission to make use of the notes relating to Case 5.

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## A COMPARISON BETWEEN THE MANTOUX INTRADERMAL TEST AND THE TUBERCULIN PATCH TEST

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Mass tuberculin surveys in South Africa are fraught with many difficulties, more particularly amongst the Bantu in rural areas. It has been the experience of the senior author (B. A. D.) in field investigations amongst the Bantu in Natal that the native regards with suspicion any kind of injection that he is given, particularly if he feels in good health. We have also found in investigations carried out on non-European children that many of the parents are averse to their children having injections, which are often traumatising.

For these reasons it was decided to carry out the following study to evaluate the efficacy of the Patch Test as compared with that of the Intradermal Tuberculin Test and to note their comparison on a dark (non-European) skin. A typical Indian school was chosen and about 200 boys, ranging in ages from nine to sixteen years, were examined.

### Procedure of Examination

(a) *The Patch Test.*—The patch tests used were the ordinary tests devised by Vollmer, and the site chosen for the application was on the back between the scapulæ, just lateral to the spine. The area was cleansed with ether and the patch test applied. After forty-eight hours the patch was removed and the test read. If there was no positive reaction the test was read again forty-eight hours later (*i.e.*, ninety-six hours after application).

(b) *The Mantoux Intradermal Test.*—The boys were divided into two groups. The one group was given the intradermal test with 0.1 c.c. Koch's old tuberculin; the other, purified protein derivative (P.P.D.), 0.1 c.c. of  $\frac{1}{3}$  dilution of second strength. The reason for our using the  $\frac{1}{3}$  dilution of the second strength was that on previous occasions we have found that, whereas the first strength gave a completely negative reaction, the second strength repeated on the same individual gave a very severe reaction indeed.

The Mantoux intradermal test was done on the left forearm at the same time as the patch test was applied and read when the patch was removed (after forty-eight hours). To prevent any bias in the interpretation one of us read the patch tests, while the other read the intradermal tests, and the results were correlated at the end of the study.

*Interpretations of Reactions.*—The intradermal test was considered positive when it showed an erythematous area of induration; the patch test when it showed a follicular area with underlying erythema and induration, roughly demarcated by the square patch of tuberculin-soaked material. Where any doubt arose from the reading of the patch test or from confusion due to the contact dermatitis (from the plaster) the test was again read after forty-eight hours.

### Results

(a) Comparison of patch test and intradermal test, using Koch's old tuberculin:

Total No. done	...	...	...	...	...	...	...	...	101
No. Negative on both Patch and Mantoux after forty-eight hours	...	...	...	...	...	...	...	...	80
No. Positive on both Patch and Mantoux after forty-eight hours	...	...	...	...	...	...	...	...	20

In 1 case the Patch test was negative but the Mantoux positive. (This boy had the Patch test applied on the forearm because of a skin lesion on the back.)

Contact Dermatitis (Plaster) occurred in 17.

Of these, 15 occurred in those with both Patch and Mantoux negative;  
2 occurred in those with both Patch and Mantoux positive

(b) Comparison between patch test and intradermal test (using P.P.D.  $\frac{1}{2}$  dilution of second strength):

Total No. done	...	...	...	...	...	...	...	...	78
No. Negative on both Patch and Mantoux after forty-eight hours	...	...	...	...	...	...	...	...	53
No. Positive on both Patch and Mantoux after forty-eight hours	...	...	...	...	...	...	...	...	17

In 8 cases after forty-eight hours the Mantoux was positive but the Patch test negative. These were read again after a further forty-eight hours. Of this total of 8 Patch tests 6 became positive and 2 remained negative.

Summarising, of total of 78—

No. negative in both tests	...	...	...	...	...	...	...	...	53
No. positive in both tests	...	...	...	...	...	...	...	...	23
No. with negative Patch and positive Mantoux	...	...	...	...	...	...	...	...	2

Contact Dermatitis (Plaster) occurred in 5.

Of these, 4 occurred in those with Patch and Mantoux positive and 1 occurred in those with both Patch and Mantoux negative.

### Conclusions and Comments

Though the number of children investigated is not large (under 200) our results do show the high degree of correlation between the patch and the Mantoux intradermal test. It is our opinion also that of the two substances used for the intradermal test the P.P.D. is the more sensitive.



All the tests were done on Indian children and we experienced no difficulty in reading the reactions on a coloured skin.

For mass surveys, particularly in children, the patch test is undoubtedly the method of choice. The ease of application, the high degree of accuracy, the psychological effect of not using syringes and needles, and the absence of trauma, are advantages which ought greatly to recommend this method and to popularise its more widespread use.

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## CHOLESTEROUS PLEURAL EFFUSION

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THAT the deposition of cholesterol crystals in pleural effusions must be regarded as one of the rarest complications is revealed by the scarcity of recorded cases, no more than thirty being found in the world's literature, and of these only four or five appear to have been described in Great Britain.

Sharpe (1919) described two cases seen at the Brompton Hospital, the first being a man of thirty-four years who had had a definite effusion on the same side seven years previously. On both occasions the fluid was described as straw-coloured, but examination of the fluid withdrawn at the later aspiration showed the presence of cholesterol crystals. This case had an apical shadow and was sputum-positive. The second case was a boy of nine with a tuberculous family history, who had had an operation for empyema on the same side several years previously. Repeated aspiration of a golden-yellow fluid was followed by secondary infection, and re-drainage was performed. The fluid contained pus cells, staphylococci, and cholesterol crystals.

Monro (1927) encountered a man of thirty-four who had suffered from pleurisy on the same side a year previously, and presented himself with a chocolate-coloured effusion containing pus, blood pigment, and abundant cholesterol crystals, but no tubercle bacilli. The empyema was ultimately drained.

Schulman (1917) in the United States described a man of sixty-two with a history of pneumonia and fluid which had been once aspirated forty years previously. Aspiration of the residual fluid after this long interval yielded a few ounces of yellow, cheesy material containing cholesterol crystals. The sputum was negative for tubercle bacilli.

Stein's (1932) case had a similar history of pneumonia followed by the aspiration of fluid twenty-five years previously. On admission to hospital at the later date the fluid, which was milky, was found to contain cholesterol crystals but no tubercle bacilli. The patient died of tuberculous meningitis, and at autopsy calcification and ossification of the pleura were demonstrated.

#### Author's Case

The patient, a youth of nineteen, gave a history of having had two years previously a right-sided pleural effusion, for which he was treated in hospital for two months, after which he spent ten months (four months in bed) at home before returning to work. Three weeks before admission to the sanatorium in 1940 he suffered from an attack of bronchitis and laryngitis, which entailed two or three days in bed. At the time he was informed that he had fluid on the right side again. On admission he complained of slight cough and sputum, and aching in the right loin. The physical signs were consistent with a diagnosis of right-sided effusion and the presence of a pleural opacity was confirmed radiologically, there being also some hard infiltration in both upper zones. The sputum was repeatedly negative on direct examination, but tubercle bacilli were later demonstrated by culture. An early tuberculous laryngitis, chiefly involving the arytenoids, was also present. Diagnostic aspiration revealed the presence of fluid, 500 c.c. of which were forthwith withdrawn and replaced by air. Microscopically the fluid was clear, but had a golden sheen, which proved microscopically to be due to large numbers of cholesterol crystals. Subsequent radiological examination showed that the apex was totally adherent, and that there was a small amount of fluid present, above which there appeared to be a fibrin body. As there seemed to be no special indication for maintenance of the pneumothorax, routine sanatorium treatment was decided on, but, in the belief that he could be treated at home, the patient discharged himself after a few weeks. His temperature and pulse were normal while he was at the sanatorium, his blood pressure and urine were normal, and blood cholesterol fell within normal limits at 128 mgm. per 100 c.c.

#### Biochemistry and Pathogenesis

It was found by Desbordes and Lévy (1938) that as effusions became old *in situ* the albumen-globulin ratio diminished, whilst the total protein remained constant—*i.e.*, there was an increase of globulins. *Pari passu* the cholesterolytic power of the fluid decreased, and a precipitating tendency developed. Desbordes (1938) quotes the work of Mauriac and his pupils, who, in provoking in the rabbit a strong hypercholesterolaemia, obtained,



without notable lowering of proteins, an evident lowering of albumen with corresponding inversion of the albumen-globulin ratio. Desbordes comes to the conclusion, therefore, that a part of the cholesterol exists in the state of a complex associated with the albumen-globulin combination, this liaison apparently being related to the globulins, the albumen contributing to the holding in solution of the cholesterol.

Bruger (1934) found that there was no relation between the total cholesterol content of pleural and ascitic fluids and that of the blood. This has been a general finding, which is further confirmed by the case here described, and is quite consistent with the views advanced by Desbordes.

It would seem that when the exudate is formed it contains cholesterol derived from the blood stream, but held in solution by some complex balance between the protein elements which also originate from the blood. As the fluid ages the globulin increases, the albumen decreases, and a cholesterol phanerosis develops in the form of crystals giving the golden sheen observed in several of the recorded cases. The deposition of cholesterol crystals seems, therefore, to occur by reason of senescence only, and may be expected in any pathological fluid of considerable maturity, provided that it is sufficiently isolated from the circulating body fluids to prevent any interchange of the constituents concerned in the process. Two factors are concerned in the sequestration of such fluids: firstly, protracted exudation, and secondly, as a result of such protracted formation of fluid, progressive thickening of the enclosing membrane and consequent delay in the normal process of resorption. Cardiac and renal effusions are apt to be terminal complications of the underlying disease, so that they seldom provide the conditions necessary to cholesterol deposition, but nevertheless crystals have been observed in pericardial and ascitic effusions. By virtue of its chronicity pulmonary tuberculosis is the disorder most calculated to evoke such cholesterosis, and there is reason to suspect a tuberculous basis in most of the published cases of cholesterous pleural effusion, even though tubercle bacilli have not been demonstrated.

#### Treatment

Repeated aspiration has been advocated by Stein (1932) for the relief of respiratory embarrassment, but the chronic nature of these fluids suggests that a single aspiration should be sufficient unless it is considered feasible to eliminate the fluid entirely by further aspiration. As secondary infection has supervened in some of the cases treated by frequent aspiration, the undesirability of this as a routine procedure becomes evident. When secondary infection is discovered, drainage usually becomes necessary, though ultimate apposition of the thickened or calcified pleural surfaces is

uncertain without surgical assistance. In such cases, as in every empyema, reduction in the size of the infected pleural cavity should be recorded by means of the injection of some opaque medium such as iodised oil or a barium suspension, and complete obliteration proved before the tube is withdrawn.

To return to the method of repeated aspiration, the chief field for this treatment seems to be as a prophylactic measure, and persistent effusions should be so treated, but the rarity of the risk to be avoided should deter one from the wanton aspiration of all tuberculous effusions and the very real dangers attendant on such a procedure.

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## NATURALLY OCCURRING TUBERCULOSIS IN DOGS AND SOME OTHER SPECIES OF ANIMALS

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### PART II. ANIMALS OTHER THAN DOGS

IN a previous number Lovell and White (1940) recorded the pathology and bacteriology of 22 cases of natural tuberculosis in dogs. Other species of animals have also been investigated, though it was not always possible to obtain adequate data concerning the specimens received, some of which were unopened carcasses and some selected pieces of tissue. Two cats, two sheep, one goat, three mink, one silver fox, five horses, and a sample of the meat fed to some mink and silver fox were examined.

The technique was similar to that used in dealing with the dogs.

#### Cats

The incidence of the disease in cats varies; although details of two cases only are given we have met with 4 cases among 110 cats examined *post mortem*, a percentage of 3.6. Griffith (1926) quotes the recorded incidence of three

workers: Abel, 9 of 400 cats, Petit, 2 per cent. of 366, and Yost, 110 of 933. Dobson (1930) found 11 cases of tuberculosis among 505 cats, and Nieberle (1932) 18 among 241.

*Pathology.*—The primary lesion is probably found most frequently in the alimentary tract. Of the 110 cases recorded by Yost (1921) the lesions in 30 were confined to the mesenteric nodes, and in a further 19 there was, in addition, miliary tuberculosis of the lungs. Lesions were limited to the lungs and bronchial nodes in 25 and confined to the former in 11 animals. Of 6 cases described by Griffith (1924) 5 were alimentary in origin, and in 4 more (Griffith, 1928) one involved primarily the mesenteric nodes and Peyer's patches of the intestine with generalisation, one was confined to the lungs and bronchial nodes, the third was limited to the mandibular lymph node, which had ulcerated, and the fourth involved a mandibular, mesenteric and bronchial node, the lungs, liver and spleen. Dobson (1930) considered 10 of his 11 cases to be alimentary; and Hjärre (1939) records 20 cases, of which 10 were thought to be alimentary, 8 respiratory and 2 cutaneous in origin. Innes (1940) describes 13 cases, the primary lesions in each being in the alimentary tract. In contrast with this Nieberle (1931) gives a high incidence of primary tuberculosis of the respiratory tract—namely, 13 of 18 cases.

As in the dog, calcification and giant cells of the Langhans type are rarely seen.

*Bacteriology.*—In the two cats dealt with, tubercle bacilli were isolated by direct means, and both were dysgonic bovine in type. In Table I are given records of the types of tubercle bacilli isolated from cats; from 52 of 56 the organism was of the bovine type. Rabinowitsch-Kempner (1921) records 3 cases due to the human type; her material was received from Yost (1921), who practised in Berlin and examined macroscopically thousands of dogs and many hundreds of cats. It is not possible to say whether mistakes were made, but Griffith (1926) considers that, in cats, no authenticated example of infection with the human type has been found. Cobbett (1907), working for the Royal Commission, found the cat highly resistant to infection with this type, and similar results have been obtained by Kuwabara (1938). The strain recorded by Hjärre (1939) as of human type was not tested culturally but only by the inoculation of rabbits and guinea-pigs (Hjärre, private communication). It appears that the cat—unlike the dog—is not equally susceptible to both mammalian types of tubercle bacilli.

TABLE I.—TYPE OF TUBERCLE BACILLUS ISOLATED FROM NATURAL CASES OF TUBERCULOSIS IN CATS

Country.	Author.	Type.			No. Exd.	
		Human.	Bovine.	Avian.		
England ... ..	Griffith, F., 1911		1		1	One of low virulence
	Cobbett, 1926		3		3	
	Griffith, A. S., 1926		12		12	
	Griffith, A. S., 1928		4		4	
	Stableforth, 1929		5		5	
Scotland ... ..	Dobson, 1930		11		11	Incomplete examination Findings adversely criticised
U.S.A. ... ..	Smith, 1905		2		2	
Germany ... ..	Rabinowitsch-Kempner, 1921	3	3		6	
Italy ... ..	Foresti, 1936		1		1	
Norway ... ..	Hjärre, 1939	1	6		7	
Switzerland ... ..	Galli-Valerio and Bornand, 1921		2		2	
England ... ..	Here recorded		2		2	

### Sheep

Specimens from two tuberculous sheep were examined. In one case (No. 1) the animal had been bred on a farm with an accredited herd of dairy cattle (there were no pet or hand-reared lambs and no pigs or poultry). Sheep had not been grazed on land used by the cattle for two years previously, but twice during recent months the flock had broken through into fields of an adjacent farm where pigs and poultry were kept. A eugonic bovine type of tubercle bacillus of standard virulence was recovered from the lungs by guinea-pig inoculation. The second sheep (No. 2) had been bought in the open market for slaughter and had come from a farm where a cow had recently "wasted away" and fowls were "pining" and dying. What association there is between the sheep and fowls is difficult to say, but the sheep had access to land where the cow and poultry had been, and a dysgonic bovine type of tubercle bacillus was isolated from an hepatic lymph node by direct means.

Table II shows that the bovine type is commonly the cause of ovine tuberculosis, but that since 1925 several workers have recorded the isolation of the avian type from sheep, especially in the U.S.A. For example, the Meat Inspection Division of the Bureau of Animal Industry (U.S.A.) (1938) condemned during the fiscal year ending June 30, 1938, 42,180 of 17,676,408 sheep and lambs examined. Of these 18 were for tuberculosis. Tissues

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from 17 sheep suspected of tuberculosis were examined by the Pathological Division and the avian type was recovered from 14. Two were tuberculous by histological examination and one parasitic. One case due to the human type has been reported from Uganda (Carmichael, 1938).

TABLE II.—TYPE OF TUBERCLE BACILLUS ISOLATED FROM NATURAL CASES OF TUBERCULOSIS IN SHEEP

Country.	Author.	Type.			No. Exd.	
		Human.	Bovine.	Avian.		
England ...	M'Fadyean, 1900		1		1	No cultural tests
	M'Fadyean, 1902		1		1	
	Griffith, A. S., 1925			2	2	One strain atypical
Scotland ...	Jowett, 1928		2		2	
Ireland ...	Murphy, 1935		1		1	No cultural tests
	Craig and Davies, 1938		1		1	Imported from Ireland
U.S.A. ...	Mohler and Washburn, 1907		1		1	
	van Es and Martin, 1930		1		1	
	Harshfield and Roderick, 1934			7	7	
	Harshfield <i>et al.</i> , 1937			18	19	One possibly bovine
	Bur. of An. Ind., 1938			14	16	Two by histology
	Stubbs and Live, 1939		1		1	
	Carmichael, 1938	1	10		12	Organism not recovered from 1 case
Italy ...	Giudice, 1935		1		1	Reduced virulence
England ...	Here recorded		2		2	One eugonic bovine

## Goats

One specimen from a goat was examined, and from it was isolated a dysgonic bovine type of tubercle bacillus. Very scanty history was available, and a portion of the lungs only was received from a veterinarian who wished for confirmation of his diagnosis of tuberculosis.

Table III shows that with one exception tubercle bacilli obtained from goats have been of the bovine type. Although it is probable that goats are usually infected from tuberculous cattle it is shown by Bishop *et al.* (1934) that a tuberculous goat may be of danger to cattle, for a newly purchased goat was responsible for the introduction and subsequent spread of tuberculosis in a herd of cows.

TABLE III.—TYPE OF TUBERCLE BACILLUS ISOLATED FROM NATURAL CASES OF TUBERCULOSIS IN GOATS

Country.	Author.	Type.			No. Exd.	
		Human.	Bovine.	Avian.		
England ...	Griffith, A. S., 1917		1		1	No cultural test
	Griffith, A. S., 1936			1	1	
	Schwabacher, 1934		1		1	
U.S.A. ...	Bishop <i>et al.</i> , 1934		1		1	
Germany ...	Zwick, 1908		3		3	No details of tests given
	Rabinowitsch-Kempner, 1921		1		1	
Uganda ...	Carmichael, 1938		10		10	
South Africa	Fourie, 1928		1		1	
England ...	Here recorded		1		1	

### Mink and Silver Fox

During the years 1937 and 1938 a total of 40 mink were examined at the laboratory. Of these animals, some died and were received without having been first pelted, others were killed and pelted because of illness, and a few were sent in after pelting although there was no suggestion of disease. Among this selected population, coming from four different farms, there were 17 cases of tuberculosis, of which 3 were examined bacteriologically.

Of the 17 tuberculous mink, 15 died from generalised tuberculosis, 1 from intussusception of the small intestine, and 1 was destroyed because of loss of condition. In 7 animals the primary lesion appeared to be in the mesenteric lymph nodes, with miliary tuberculosis of the lungs and involvement of other organs, including the liver, kidneys, adrenals and spleen. In 2 mink the primary lesion was in the mandibular lymph node, with secondary miliary lesions in the lungs. In the remaining 8 mink it was not possible to identify macroscopically the primary lesion, but in each case there was miliary tuberculosis of the lungs. There was a tuberculous peritonitis in 6 cases. In 1 mink the first symptom observed during life was a watery and later purulent discharge from the left eye. A few days before death the animal lost condition rapidly and there was repeated vomiting. Death occurred 18 days after the ocular discharge was first noticed. At autopsy there was tuberculosis of the mesenteric lymph nodes, miliary tuberculosis of both lungs, and extensive tuberculosis of the left eye.

A common finding is the enormous numbers of tubercle bacilli in smears, and the peritoneal lesions are also characteristic. There are greyish plaques on the parietal peritoneum, especially over the diaphragm, with a small

quantity of greyish glutinous fluid in the peritoneal cavity containing many tubercle bacilli; a tuberculous pleurisy was not observed.

Histological sections of a Peyer's patch in a mink with tuberculosis of the mesenteric glands showed the villi packed with epithelioid cells containing a great number of bacilli. There was a tuberculous lymphangitis in the submucosa and subserosa.

Two cases of tuberculosis were also encountered among 19 silver foxes examined *post mortem*. From one of these a culture of tubercle bacilli was isolated by a colleague by guinea-pig inoculation. The animal had been gradually losing condition, would take no food, and died. The post-mortem examination showed advanced tuberculosis, and the bacillus isolated was a eugonic bovine type of standard virulence.

The histological features of tuberculosis in fur-bearing animals have been described by Nieberle (1935), but records of the bacteriology of the disease in these animals are few. In each case recorded (Table IV) the infecting organism has proved to be of the bovine type. It is the custom of breeders of many fur-bearing animals to feed them with raw meat in order to develop a good coat. The dangers of this procedure are obvious, and Kingscote (1936) records the reduction in tuberculosis in mink when attention is paid to the meat supply. An examination of the food was made in one instance, and the recorded data need no comment. A portion of raw beef was sent in by a mink and silver fox farmer from whom seven tuberculous mink had been received. The sample consisted of a piece of muscle measuring 6×4×4 cm. to which was attached a caseous lymph node. The specimen was taken from the meat, which was fed in the raw state to silver foxes and mink on the farm. Acid-fast organisms were found in smears from the lymph node and tubercle bacilli were isolated by a colleague by inoculation

TABLE IV.—TYPE OF TUBERCLE BACILLUS ISOLATED FROM NATURALLY OCCURRING CASES OF TUBERCULOSIS IN MINK AND SILVER FOX

Country.	Author.	Type.			No. Exd.	
		Huam.	Bovine.	Avian.		
Mink:						
England ...	Griffith, 1936		1		1	
Canada ...	Kingscote, 1936		2		15	Only 2 examined bacteriologically Only 3 cultured from
England ...	Here recorded		3		17	
Silver Fox:						
U.S.A. ...	van Es and Martin, 1930		1		1	
England ...	Here recorded		1		1	Eugonic bovine



of guinea-pigs. The strain grew poorly on egg and serum, with no improvement on glycerin media. Two guinea-pigs given 0.1 mgm. of a culture died from generalised tuberculosis after 41 and 45 days respectively. Two rabbits which received 1.0 mgm. died after 49 and 55 days respectively. It was considered to be a dysgonic bovine type.

### Horses

Five cases of tuberculosis in the horse have been studied, and the infecting bacillus was isolated by direct methods from three and by the use of guinea-pigs from the other two. The strains were all of the bovine type, three being of reduced virulence.

*Pathology.*—In the horse primary infection is usually alimentary, the lesions being commonly confined to the mesenteric lymph nodes; this is followed in most cases by generalisation. In the lungs the lesions consist of greyish, translucent miliary tubercles or, in some cases, larger confluent areas with a caseous centre. The spleen is often involved, with the formation of large tumour-like masses usually without macroscopic caseation. The serous membranes may show plaque-like lesions or a more diffuse tuberculous serositis.

TABLE V.—TYPE OF TUBERCLE BACILLUS ISOLATED FROM NATURAL CASES OF TUBERCULOSIS IN HORSES

Country.	Author.	Type.			No. Exd.	
		Human.	Bovine.	Avian.		
England ...	Griffith, F., 1911		5		5	Two of reduced virulence
	M'Fadyean, 1918			1	1	Abdominal type disease
	M'Fadyean, 1924		11		11	Probably 4 reduced virulence
	Griffith, 1928		8		8	5 strains of reduced virulence
	Stableforth, 1929		13		13	6 strains of reduced virulence
	Griffith, 1936	1			1	
	Griffith, 1937		16		16	7 below standard virulence
U.S.A. ...	van Es and Martin, 1930		2		2	
Germany ...	Zwick, 1908			1	1	Probably avian
	Zwick and Zeller, 1913		8		8	
France ...	Nocard, 1896			1	1	
Denmark ...	Werdelin, 1935		1	2	3	
England ...	Here recorded		5		5	3 reduced virulence

Subendocardial calcification is a fairly common finding, and it has been claimed that tubercle bacilli can be isolated from these areas. The changes represent a dystrophic calcification of the vessel wall in relation to the elastic fibres, and there is no cellular reaction. It has been recorded in the horse in conditions other than tuberculosis.

In the liver, amyloid deposition is sometimes seen, and tuberculosis of the bones frequently occurs in generalisation. Schmidt (1930), for example, found bone lesions in 25 of 200 tuberculous horses examined *post mortem*.

**Bacteriology.**—Almost all cases of tuberculosis in the horse are due to the bovine type (Table V) and about half of the strains are of reduced virulence. This is a well-known observation and has been pointed out many times. There are a few cases recorded of tuberculosis due to the avian type. One case due to the human type has been described by Griffith (1936).

### Summary

A study of natural tuberculosis in several species of domestic animal is recorded, and the pathological and bacteriological findings discussed.

The number of animals examined and the type of infecting bacillus are as follows:

Cats	...	...	...	...	2 (both bovine)
Sheep	...	...	...	...	2 (both bovine)
Goat	...	...	...	...	1 (bovine)
Mink	...	...	...	...	3 (all bovine)
Silver fox	...	...	...	...	1 (eugonic bovine)
Horse	...	...	...	...	5 (all bovine, 3 of reduced virulence)

We are indebted to Dr. F. C. Minett for his records relating to the strains isolated from horses; and to Mrs. Seymour Smith, M.R.C.V.S., who made the primary isolations from the fur-bearing animals.

## APPENDIX

### CATS

No. 1.—Three-years castrated male. History of 14 days' dullness, inappetence and loss of flesh. Temperature 100° F. Large irregular mass palpated in the position of the mesenteric lymph nodes. Destroyed.

**Autopsy.**—Peritoneal cavity contained 400 c.c. pale yellowish fluid with whitish flocculi; glutinous deposit on standing, with numerous clumps of acid-fast organisms in smears. The mesenteric nodes formed a mass measuring 5×4×3 cm., enveloping several loops of intestines, and on section was greyish with numerous small cystic spaces containing pus rich in acid-fast organisms. Parietal and visceral peritoneum covered with a thin greyish film of deposit which was easily scraped off, leaving a smooth serous surface. There were no other macroscopic lesions.

**Bacteriology.**—Strain isolated direct from enlarged mesenteric node grew only moderately well on egg, with a faint growth on serum; no improvement on glycerin media. Two guinea-pigs died from generalised tuberculosis 38 and 44 days respectively after inoculation with 0.2 mgm. of a second-generation culture and two rabbits 36 and 65 days respectively after inoculation with 2.0 mgm.

Dysgonic bovine type.

No. 2.—Four to five months male. History of several weeks' respiratory distress and failure to gain weight. Destroyed.

*Autopsy.*—About 200 c.c. of fluid in pleural cavities and fibrinous deposit on pleura. Lungs mostly consolidated, presenting yellowish-grey marbled appearance; on section, several small cavities containing yellowish pus. Bronchial nodes were not enlarged but showed two minute greyish foci on section. Acid-fast bacilli numerous in smears of lung lesions.

*Bacteriology.*—Culture recovered direct from lung lesions grew poorly on egg and serum, with no improvement on glycerin media. Two guinea-pigs died from generalised tuberculosis 49 and 50 days respectively after inoculation of 0.1 mgm. of a second-generation culture and two rabbits 51 and 53 days after inoculation of 1.0 mgm.

Dysgonic bovine type.

#### SHEEP

No. 1.—The material comprised a portion of the lungs and bronchial and mediastinal lymph nodes of a lamb, showing multiple caseated and calcified lesions. A few acid-fast bacilli were found in smears from the lung and lymph node lesions. A few days later the carcass, together with the adrenals, right kidney, mesenteric lymph nodes, and liver, was obtained, but no macroscopic lesions of tuberculosis were found.

*Histology.*—Lesions were similar to those in cattle—namely, caseation, very considerable calcification, a periphery of epithelioid cells, and lymphocytes with a number of giant cells of the Langhans type.

*Bacteriology.*—Strain recovered from guinea-pig inoculated with emulsion of lung lesions grew fairly well on egg and serum, with slight improvement on glycerin media. A guinea-pig inoculated with the original material died from generalised tuberculosis in 69 days; of two guinea-pigs given 0.2 mgm. of a second-generation culture, one died in 8 days from intercurrent disease and the other in 35 days from generalised tuberculosis. Two rabbits injected with 2.0 mgm.—one died after 45 days and the other killed in a moribund condition after 47 days, both with generalised tuberculosis.

Eugonic bovine type of standard virulence.

No. 2.—The material comprised the "pluck" and kidneys of a ewe suspected of tuberculosis. No macroscopic lesions of tuberculosis had been observed in tissues other than those sent to the laboratory.

The mediastinal node showed a few small calcified foci. The liver contained numerous whitish foci 1 to 2 mm. in diameter and a larger caseous lesion 1 cm. in diameter. The bronchial nodes were normal. The lungs were studded throughout with small greyish translucent nodules probably caused by strongyle larvæ. No acid-fast bacilli were found in smears.

*Histology.*—Lung lesions showed structure typical of those caused by strongyles; there was no evidence of tuberculosis. The liver lesions consisted of small aggregations of epithelioid cells and lymphocytes, mainly periportal in position, with occasional giant cells of the Langhans type. Caseation was seen only in the large lesion.

*Bacteriology.*—Culture obtained direct from hepatic node grew poorly on egg and serum, with no improvement on addition of glycerin. Two guinea-pigs given 0.2 mgm. of a second-generation culture died after 33 and 47 days respectively, and two rabbits injected with 2.0 mgm. died after 37 and 47 days respectively, all from generalised tuberculosis.

Dysgonic bovine type.

#### GOATS

A portion of the lungs only was received; this was in an advanced state of decomposition and consisted mainly of innumerable yellowish-white lesions, with a small amount of fairly normal intervening lung tissue. Acid-fast organisms were very numerous in smears.

*Histology.*—Tubercles with central caseation and calcification were seen throughout the lung tissue; giant cells of the Langhans type were present in considerable numbers.

*Bacteriology.*—Strain isolated from a guinea-pig inoculated with emulsion of the lung tissue of the goat grew poorly on egg and serum, with no improvement on the addition of glycerin. Two guinea-pigs inoculated with 0.2 mgm. of a second-generation culture died from generalised tuberculosis after 46 and 49 days respectively; two rabbits given 2.0 mgm. died after 44 and 54 days respectively.

Dysgonic bovine type.

## MINK AND SILVER FOX

MINK No. 1.—Primary tuberculosis of the mesenteric lymph nodes with generalisation was found at autopsy.

*Bacteriology.*—Strain isolated by a colleague grew poorly on egg and serum, with no improvement on glycerin media. Two guinea-pigs died from generalised tuberculosis 41 and 51 days respectively after the injection of 0.1 mgm. of a culture. Two rabbits were given 1.0 mgm.—one died after 34 days with progressive tuberculosis, although the immediate cause of death was not determined; the other rabbit died from generalised tuberculosis after 39 days.

Dysgonic bovine type.

MINK No. 2.—Tuberculosis of the mandibular lymph nodes, miliary tuberculosis of the lungs and tuberculous peritonitis found at autopsy.

*Bacteriology.*—Strain isolated by a colleague grew poorly on egg and serum, with no improvement on glycerin media. Two guinea-pigs died from generalised tuberculosis 37 and 49 days respectively after inoculation with 0.1 mgm. of culture. Two rabbits died from generalised tuberculosis 44 and 46 days respectively after receiving 1.0 mgm.

Dysgonic bovine type.

MINK No. 3.—Tuberculosis of the mesenteric nodes, miliary tuberculosis of the lungs and lesions in the kidneys and left adrenal.

*Bacteriology.*—Strain isolated by a colleague grew poorly on egg and serum, with no improvement on glycerin media. Two guinea-pigs died from generalised tuberculosis 46 and 59 days respectively after the injection of 0.1 mgm. of culture; two rabbits receiving 1.0 mgm. died after 45 and 55 days respectively.

Dysgonic bovine type.

SILVER FOX—*Autopsy.*—Post-mortem changes very advanced: peritoneal cavity contained 100 c.c. of blood-stained effusion; mesenteric lymph nodes enlarged and consisted of several masses measuring up to  $4 \times 2 \times 1$  cm.; cut surface greyish and a small amount of pus could be expressed. Several erosions of the mucosa of the small intestine and the intestinal contents contained a considerable quantity of blood. Liver enlarged, yellowish in colour and contained innumerable yellowish opaque lesions up to 1 cm. in diameter. Kidneys contained several greyish lesions in the cortex and medulla. Lungs studded throughout with minute greyish translucent foci. Bronchial nodes not enlarged.

*Bacteriology.*—The strain formed a slight confluent growth on egg medium, with moderate improvement on glycerin-egg; the growth was fairly dry and whitish with a few heaped-up secondary colonies. A moderate growth was formed on serum, with slight improvement on glycerin serum, the latter with faint yellowish pigmented colonies. In general the growth was better than that of a dysgonic bovine type but not so heavy as the eugonic human type. Two guinea-pigs given 0.1 mgm. of a second-generation culture died from generalised tuberculosis after 37 days. Of two rabbits given 1.0 mgm. one died from intercurrent disease after 32 days but showed widespread tuberculosis; the other died from generalised tuberculosis after 42 days.

Eugonic bovine type of standard virulence.

## HORSES

No. 1.—Eight-years mare. Loss of condition extending over a month, laboured respiration. A positive tuberculin reaction was obtained following a single intradermal injection. Animal destroyed.

*Autopsy.*—The lungs were voluminous and weighed 30 kg., with very little normal tissue; the lung tissue had been replaced by whitish lesions, from a few mm. to 3 cm. in diameter with a translucent greyish periphery and an opaque yellowish caseous centre. Bronchial nodes enlarged, but no discrete macroscopic lesions. No pleurisy. Subendocardial calcification left side of heart involving auricle, ventricle, and valves. Mesenteric nodes formed a bosselated mass weighing 2 kg. with a yellowish caseous appearance on section. The omentum and parietal peritoneum showed firm plaque-like lesions of varying size.

*Bacteriology.*—Culture obtained direct from lesions grew poorly on egg and serum, with no improvement and slower growth on glycerin-egg; less growth on glycerin serum. Guinea-pigs, rabbits, calves, and fowls were injected, and the following results are cited. Two guinea-pigs injected with 1.0 mgm. and 0.1 mgm. respectively of a third-generation culture—the former killed moribund after 34 days, latter died after 59 days; both showed generalised tuberculosis. Three rabbits given 10 mgm., 1 mgm., and 0.1 mgm. respectively of a similar suspension—all died from generalised tuberculosis after 95, 135, and 106 days respectively. Three rabbits injected intravenously with 1 mgm., 0.1 mgm., and 0.01 mgm.—all died from generalised tuberculosis on the 34th, 65th, and 41st day respectively. One calf injected subcutaneously with 30 mgm. died from miliary tuberculosis after 55 days; another calf given 10 mgm. was killed after 138 days with extensive and widespread tuberculosis. Two fowls injected intravenously with 1 mgm. and 0.01 mgm. were normal when killed after 290 days.

Dysgonic bovine type of reduced virulence.

No. 2.—Nine-years Shire horse. Three months prior to examination reported to be unthrifty; temperature always 102° F. or higher. Animal turned out to grass for a month, and slight improvement in condition followed. A fortnight before admission the animal developed a cough, temperature 102 to 103° F. Destroyed.

*Autopsy.*—The spleen, a portion of liver, one lung, several lymph nodes, and a portion of diaphragm were received at the laboratory. Spleen showed several greyish, tumour-like lesions 4 to 5 cm. in diameter, numerous plaques on surface of liver; lung studded with innumerable greyish translucent tubercles, confluent in places, more than half of the tissue being tuberculous. Mesenteric nodes enlarged and caseous; bronchial nodes slightly enlarged but no macroscopic tuberculosis.

*Bacteriology.*—Strain isolated from guinea-pig inoculated with emulsion of spleen nodule grew slowly on egg, with poor growth on glycerin-egg. Two guinea-pigs died from generalised tuberculosis 31 and 40 days after subcutaneous injection of 1 mgm. and 0.1 mgm. respectively of a first-generation culture. Two rabbits died from generalised tuberculosis 24 and 30 days after receiving 0.1 mgm. and 0.01 mgm. intravenously.

Dysgonic bovine type of standard virulence.

No. 3.—Eight-years gelding, first noticed to be losing condition six months previously; three weeks before examination stiffness of the neck noticed by the farmer. A marked positive reaction was obtained after a single intradermal injection of tuberculin. Animal destroyed.

*Autopsy.*—The lesions observed by the veterinary surgeon who conducted the examination comprised: several greyish nodules in the spleen, enlargement of the mesenteric, bronchial, and mediastinal lymph nodes, and tuberculous lesions in the bodies of the 10th to 13th cervical vertebrae.

*Bacteriology.*—Strain isolated from lesions in spleen and mesenteric lymph node by use of antiformin. Growth slow on egg, with less growth on glycerin-egg. Two guinea-pigs receiving 0.1 mgm. and 1 mgm. of a third-generation culture died after 80 and 113 days respectively—the first from generalised tuberculosis, the second from an intercurrent disease; two receiving 0.1 mgm. and 1 mgm. of a fifth-generation culture died after 45 and 46 days respectively from tuberculosis which was not advanced. Two rabbits inoculated intravenously with 0.01 mgm. and 0.1 mgm. died after 132 and 113 days respectively, the first showing widespread tuberculosis and the second generalised tuberculosis. Two further rabbits died with widespread tuberculosis 146 and 117 days after the intravenous injection of 0.01 mgm. and 0.1 mgm. respectively of a fifth-generation culture.

Dysgonic bovine type of reduced virulence.

No. 4.—Six-years vanner mare. Loss of condition during six months prior to examination. Subcutaneous tuberculin test negative three weeks before slaughter.

*Autopsy.*—Extensive medial and intimal calcification of aorta and pulmonary artery and subendocardial calcification of left auricle and ventricle. Calcification at origin of aorta extending along coronary arteries as far as their smaller ramifications. Lungs voluminous, inferior portion of all lobes was normal, tuberculous lesions being confined to superior parts. The most severely affected areas of the upper part of the lungs consisted of a yellowish tissue with no sign of normal lung; more inferiorly there were small areas of fairly normal lung separated by greyish translucent lesions, the larger ones having a yellow

## TUBERCULOSIS IN DOGS AND OTHER ANIMALS 39

caseous centre. Left lung weighed 9.5 kg. (normal weight=3.5 kg.). Mediastinal and bronchial nodes were enlarged and caseous. Ileum contained an ulcer 2.5 cm. in diameter situated 120 cm. from ileo-caecal valve. Spleen showed four spherical greyish nodules with caseous centres. Acid-fast organisms numerous in smears.

**Bacteriology.**—Strain recovered from lesions by use of antiformin grew poorly on plain egg, with no improvement on glycerin-egg. Two guinea-pigs inoculated with 1 mgm. and 0.1 mgm. respectively of a first-generation culture—the former died after 31 days and the latter after 40 days, both from generalised tuberculosis. Two rabbits inoculated intravenously with 0.1 mgm. and 0.01 mgm. respectively—the former died after 28 days and the latter after 41 days, both from generalised tuberculosis. A fowl inoculated intravenously with 0.1 mgm. died after 52 days; there were no lesions, but there were surviving tubercle bacilli in the spleen, shown to be of bovine type.

Dysgonic bovine type.

No. 5.—Six-years pony gelding. Indefinite history of loss of condition. Destroyed.

**Autopsy.**—Left kidney adherent to spleen, to which it was attached by a firm mass of tissue measuring 20 × 15 × 15 cm. This mass comprised a spleen nodule and the sublumbar and renal lymph nodes. The centre of the mass was caseous. Several mesenteric nodes were enlarged and caseous. Parietal peritoneum showed several firm tuberculous lesions, and there were a few similar lesions on pleural surface of diaphragm. Miliary tubercles, greyish and translucent, scattered throughout both lungs; bronchial nodes slightly enlarged. Liver contained a few lesions 3 to 5 cm. in diameter. Acid-fast organisms extremely numerous in smears of spleen and lymph node lesions.

**Bacteriology.**—Culture obtained from guinea-pig inoculated with emulsion of a spleen nodule grew poorly on egg, with less growth on glycerin-egg. Two guinea-pigs inoculated with 1 mgm. and 0.1 mgm. respectively of a second-generation culture died after 53 and 54 days respectively during cold weather, both showing slight but progressive tuberculosis. Two further guinea-pigs given 1 mgm. and 0.1 mgm. respectively of a third-generation culture—the former died after 115 days and the latter after 117 days, and both showed local tuberculosis and slight tuberculosis of the liver and spleen. Two rabbits inoculated intravenously with 1 mgm. and 0.1 mgm. respectively of the second-generation culture—the former was killed after 214 days with slight tuberculosis of the lungs and kidneys; the latter died after 164 days with slight tuberculosis of the lungs, spleen, and kidneys. A fowl inoculated intravenously with 0.1 mgm. was killed after 164 days; it was normal.

Dysgonic bovine type of low virulence.

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## CYSTIC EMPHYSEMA OF THE LUNGS WITH INTERSTITIAL SCLEROSIS

By I. CALMA,

M.D.

PULMONARY cysts develop either from the bronchial part of the respiratory system or from the alveolar structures. Here we are concerned only with the latter. We may distinguish in this group:

(1) Congenital cysts: this lesion has been found in prematurely born children by Meyer and Hueter.

(2) Emphysematous cysts: an acquired condition, since true emphysema cannot develop unless the individual has breathed.

(3) Cases of congenital malformation together with cystic emphysema. Peperé described an example in a girl, aged sixteen, in whose lungs he found



PLATE XI.



FIG. 1.—UPPER LOBE OF RIGHT LUNG ( $\times 1.5$ ).

*(To face page 40.)*

PLATE XII.

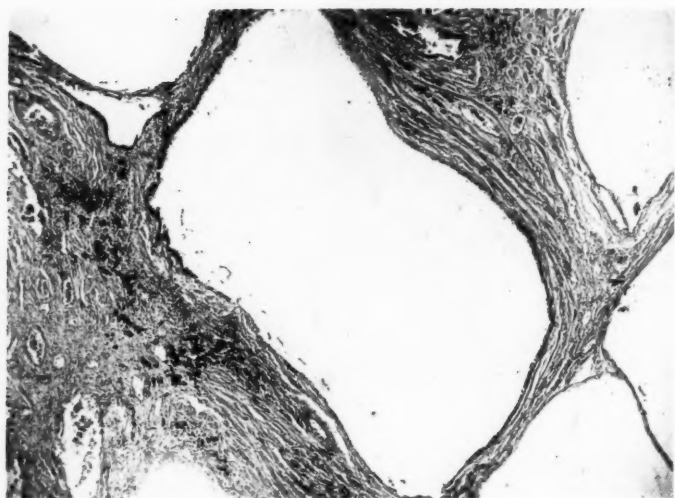


FIG. 2.—CYST IN A SCLEROTIC AREA ( $\times 20$ ).

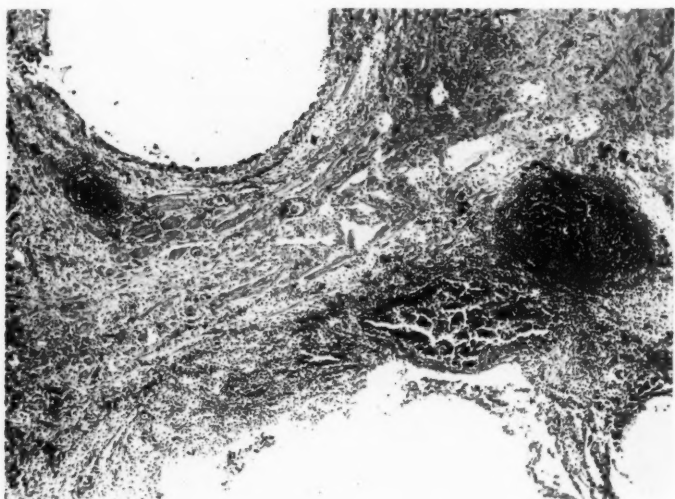


FIG. 3.—SCLEROTIC AREA WITH MANY MUSCULAR FIBRES ( $\times 20$ ).

small oblong cavities looking like embryonic alveoli and large cavities due to enlargement of normal alveoli and small bronchi. According to Pepere, this was caused by congenital weakness of elastic structures.

The following is a case of cystic emphysema which offers some points of interest.

A joiner, aged thirty-six, was admitted to hospital for a syncopal attack; he died shortly after admission and no clinical record is available. Three years before his death he was said to have had attacks like angina pectoris, ever increasing in frequency and severity.

*Post-mortem Examination.*—Antero-posterior diameter of thoracic cavity considerably larger than normal; epigastric angle strongly obtuse. Thorax: Firm adhesions over both lungs, especially on left side.

Heart: Marked hypertrophy and dilatation of right auricle and ventricle. No other change.

Aorta: Calibre slightly reduced, particularly along the ascending aorta.

Pulmonary artery: Slight dilatation with early atheroma.

Lungs: Both lungs bigger than normal, reddish-brown in colour, with little anthracosis. Elasticity markedly reduced. Some emphysematous bullæ, very marked in the upper lobes, less in the lower lobes. On the cut surface, the lungs showed a sponge-like appearance (Fig. 1) owing to the presence of cavities with a maximum diameter of 2 cm., regular borders, and fibrous shining walls, which contain small vessels and bronchi. Greatly thickened fibrous septa are present. These alterations have been found throughout both lungs, being particularly conspicuous in the upper and marginal regions.

### Histology

There is no differentiation of alveoli, infundibula and alveolar ducts. In their place large round or elongated cavities are found, with a diameter exceeding that of an acinus (Fig. 2). The walls of these cavities are formed by flat or cubical epithelium lining the thick collagenous septa. Some heart failure cells are also present. In the alveolar septa the elastic fibres are thin and fragmented, and finally capillaries only are found in the extremely atrophic septa. Among the cavities mentioned above there are large areas of collagenous tissue, without elastic fibres or with a few broken and atrophic ones (Figs. 3 and 4). We noticed that in these areas are contained many muscular fibres without any noticeable relation to the bronchial or vascular muscular coats. There are also lymphoid-like cells, sometimes diffusely spread and infiltrating the spaces between the collagenous fibres, sometimes forming round-shaped nodules, containing large reticulo-endothelial elements in the centre.

**Bronchi:** The bronchi with a diameter less than 1 mm. are surrounded by a connective-tissue coat larger than normal. Smaller bronchi show a very marked increase of peribronchiolar connective tissue; the respiratory bronchioles and alveolar ducts have disappeared and given place to round tubules with a diameter of  $\mu$  70-200, with cubic epithelium directly lining the connective tissue. They look like glandular tubules.

**Vessels:** The small vessels contained in the fibrotic areas show a great thickening of their internal coat, sometimes obliterating the lumina.

### Discussion

The chief point of interest which this case offers is the combination of cysts throughout the lungs and interstitial fibrosis.

It is not easy to differentiate pulmonary cysts of alveolar and bronchial origin. Müller actually believes that it is impossible. But the type of the lining epithelium and nature of the surrounding stroma may enable us to say in which part of the respiratory system cysts formation probably started. In the present case the following points are in favour of the alveolar origin: the lining epithelium being flat or cubic: the lack of a muscular coat and cartilage in the surrounding stroma; the absence of further alveolar parts of the acinus which could be regarded as continuations of cystic dilated bronchi. The alteration of the elastic tissue makes it clear that the alveoli underwent a dilatation of emphysematous type. It is not unlikely that we observed only the last stage of a long process of dilatation of alveoli which took place throughout life and was due to a congenital weakness of elastic structures. The cysts were bigger in those parts of the lungs most affected by respiratory expansion.

The interstitial sclerosis cannot be explained by a chronic inflammatory process. It may be the expression of an attempt by the body to build up a framework supporting the weak parenchyma—*i.e.*, the atrophic remnants of the respiratory surface. In this connection it may be remembered that a supporting function has been ascribed by Engel and Newns to the hypertrophic muscular tissue of lungs. Although in our case muscular fibres do not appear to have originated from pre-existing muscular tissue and have a different distribution from that described by Engel and Newns and Baltisberger, it is not unlikely that they have the same supporting function.

### Summary

A case of cystic emphysema with interstitial sclerosis has been described. The cystic dilatation of alveoli is probably due to congenital weakness of the elastic tissue.

PLATE XIII.

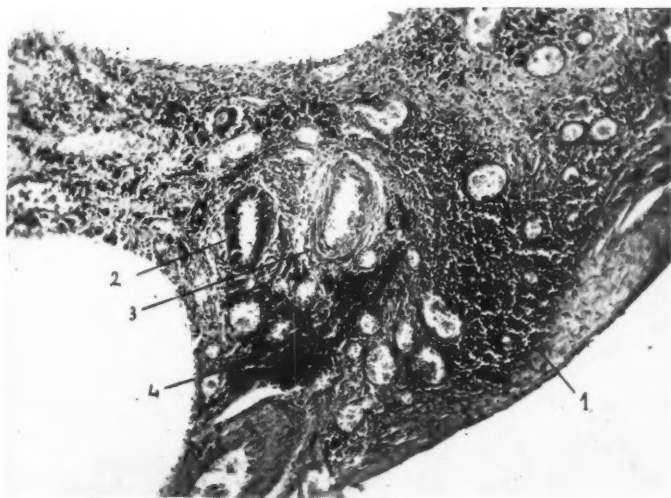
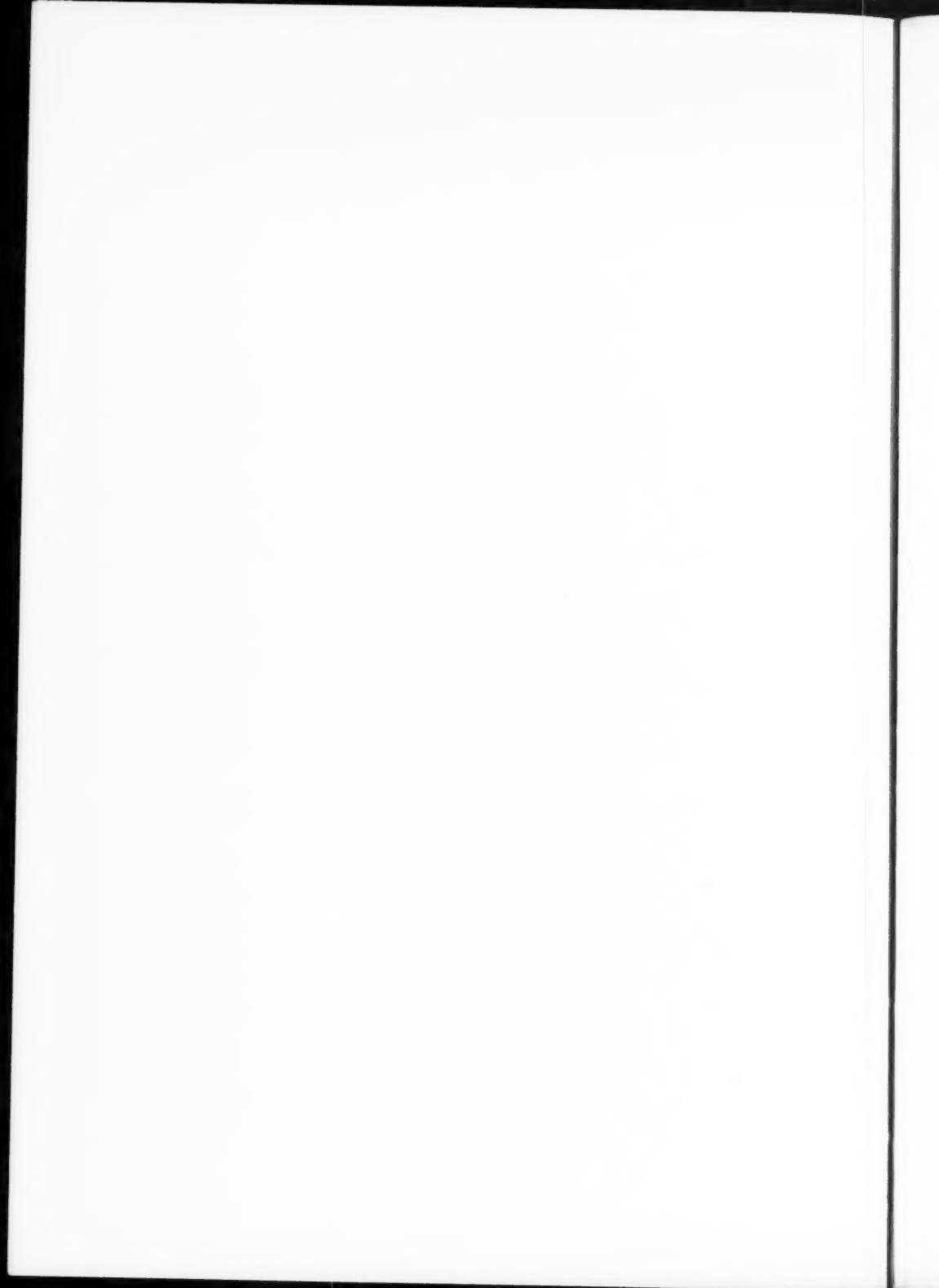


FIG. 4.—SCLEROTIC AREA WITH (1) LYMPHOID NODULE, (2) PSEUDO-GLANDULAR TUBULE, (3) SMALL ARTERY, (4) ANTHRACOSIS ( $\times 20$ ).



The fibrotic thickening may be considered as the expression of a reaction of the interstitial tissue in order to build up a supporting framework to the lungs.

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## OBITUARY NOTICE

## PENDRILL CHARLES VARRIER-JONES

## AN APPRECIATION

THE death of Sir Pendrill Varrier-Jones has deprived the medical profession of one of the most distinguished of its sons, and has removed from the ranks one of the most outstanding pioneers of the anti-tuberculosis campaign. The general character of his work, the achievement of a lifetime, is well known to our readers, as indeed it is to all who have been associated with the tuberculosis world, but the story of its inception and of the vision and determination which inspired it is less familiar. It is fitting that this JOURNAL should, in its tribute to the memory of our colleague, record its admiration for the character and foresight of the man who brought this courageous experiment through so many difficulties to such a successful achievement.

Varrier-Jones began his academic career with distinction, being a Foundation Scholar and Prizeman of St. John's College, Cambridge, where he graduated with first-class honours in the Natural Science Tripos. As a student at St. Bartholomew's, his mind inclined rather to the laboratory than to the clinical side of medicine. To many of his contemporaries in hospital he appeared more the dreamer than the man of action, and for this they would chaff him, but always with good humour and affection, for they loved him. After qualification, he held the post of House Physician at Bart.'s, and subsequently returned to Cambridge to take up research work with his old teacher, Sir German Sims-Woodhead, at whose instigation he accepted, in 1914, a post of tuberculosis officer, which was vacant for the time being owing to the dislocation caused by the war. It was from his early experience of this work that the idea originated in his mind which led to the creation and development of the great organisation with which his name is associated.



The writer can recall with much appreciation a personal conversation in which Varrier-Jones described in somewhat dramatic fashion his first realisation of the economic problems of industrial tuberculosis. The patient was an intelligent man of the working class, in whom he had found unmistakable evidence of disease in the lungs and to whom he proceeded, with all the youthful enthusiasm of the newly qualified, to give advice, on approved textbook lines, as to how life should be conducted in order to effect a cure. "I told him," said Varrier-Jones, "that he must spend most of his time in the fresh air, take plenty of good nourishing food, and, since fat was important, that he should have a liberal supply of cream with his porridge each morning." The man looked at him critically, though not unkindly, and said: "Do you know what you are talking about?" "Yes," said Varrier-Jones, a little nonplussed, "I think I do." "Well, then," said the patient, "how much cream do you suppose I can afford to buy out of 17s. 6d. a week?" It was at the close of this interview that Varrier-Jones went straight back to Sims-Woodhead and poured out his soul to him. "I told him," he said, "that we were doing the whole thing all wrong, and that our teaching in the medical schools on the treatment of tuberculosis was hopeless! Something must be done about it."

From this incident fell the seed from which was to grow, in the fulness of time, the Papworth Settlement. Many who know Papworth as it is now are perhaps unaware of all the patient spadework carried out in the little colony at Bourn, where the foundations of the great venture were laid in 1915. Here, with the co-operation of his loyal and faithful matron, and with the encouragement of the little band of professional colleagues who believed in him, Varrier-Jones persisted, in spite of discouragement and sometimes of ridicule from outsiders, in the scheme on which he had set his heart, until the colony, which prospered by the power of his organisation and by the strength of his faith, was moved to Papworth in 1918. There it has flourished, as everyone knows, despite the difficulties which from time to time must beset all institutions, and has become a model for other workers who seek to deal with the economic side of the tuberculosis problem.

In the above very brief account of the birth and growth of Papworth it is, of course, impossible to do full justice to the memory of its founder. Of those who can best testify to his remarkable personal qualities, and especially to the faith and hope inspired by contact with him, the most conspicuous examples must be sought among the countless patients who have passed through his hands and who, during their period of trial, gathered from that magical contact the strength which they so sorely needed. It is not always that the personal and individual touch is granted to those who

have the supreme gift of organisation; only too often the reverse is the case. With Varrier-Jones this was not so: a large part of his success at Papworth was due to the interest which he invariably showed in the individual patient, to whom he gave of his best, however much his mind was beset, as it almost always was, with the pressing demands of administrative and financial difficulties which in men of less imaginative mould might well have engendered an impersonal and even an unsympathetic attitude towards the sick. To him, however, no personal trouble was unworthy of attention, and his patients knew this and leaned on him as on a tower of support in their moments of weakness. To his medical colleagues in the institution he was loyal and inspiring. He chose them with discrimination, and with the discharge of their allotted duties he never interfered, though his advice and help were always ready whenever they were asked, as indeed they often were. Thus, the team was happy, and the work of Papworth was carried on in an ideal atmosphere which brought to his receptive mind that sense of satisfaction that he had so richly earned.

Varrier-Jones has gone from us, but his name and his spirit will remain, of which the Papworth Settlement is a fitting and august monument.

M. D.

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## MEETINGS OF SOCIETIES

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### JOINT TUBERCULOSIS COUNCIL

A MEETING of the Joint Tuberculosis Council was held at the Tuberculosis Offices, Oxford Road, Manchester, on Saturday, November 16, 1940. Despite difficulties in travelling, eleven members attended, with Dr. D. A. Powell in the chair.

Dr. Esther Carling's resignation from the Council was accepted with regret, and a letter was received from the Royal College of Physicians intimating that the College had decided not to appoint a representative at present on the Joint Council.

The following Committees and Conveners were appointed for the ensuing year:

*Employment and After-Care* : Drs. F. R. G. Heaf and J. B. McDougall.

The Conveners reported that the report for 1940 was nearing completion and would be circulated to members of the Committee at an early date.

*Milk* : Dr. C. O. Hawthorne.

*Nursing* : Dr. H. G. Trayer.

*Post-Graduate Study* : Dr. F. R. G. Heaf.

*Major Surgical Treatment of Pulmonary Tuberculosis—its Indications and Scope* : Mr. J. E. H. Roberts.

*Welsh Report* : Dr. D. A. Powell.

*The Institutional Treatment of Children Suffering from Pulmonary Tuberculosis* : Dr. Peter Edwards.

*Definition of Terms* : Dr. F. R. G. Heaf.

*Co-operation between Tuberculosis Organisations* : The Chairman.

*Officers for 1941.*—The following nominations were made for Officers for 1941 :

*Chairman* : Dr. D. A. Powell.

*Vice-Chairmen* : Dr. James Watt (Godalming) and Dr. Ernest Ward (Devon).

*Honorary Treasurer* : Dr. G. Jessel (Lancashire).

*Honorary Auditor* : Dr. D. P. Sutherland (Manchester).

*Honorary Secretary* : Dr. J. B. McDougall, Preston Hall, Maidstone, Kent.

*Sir Wilson Jameson.*—It was resolved to send a letter of congratulation to Sir Wilson Jameson on his appointment to the post of Chief Medical Officer to the Ministry of Health.

The Honorary Secretary gave an account of the activities of the Standing Advisory Committee to the Minister of Health, and it was decided that he should give further reports on this work from time to time.

The memorandum prepared by Dr. G. Lissant Cox on the Co-ordination of Tuberculosis Schemes of Local Authorities is to be considered at the next meeting of the Council, as would also be the question of Tuberculosis in War-Time.

Discussion took place on the education of medical students in tuberculosis. Dr. Heaf pointed out that many medical students in the London area especially were being deprived of teaching facilities in tuberculosis, and he felt that an attempt should be made to enlist the services of the tuberculosis dispensaries and sanatoria in the teaching of students during the emergency. It was resolved that a letter should be sent to the Deans of the Medical Schools in London, suggesting that students should be attached for teaching purposes to tuberculosis dispensaries and sanatoria in the districts in which they are now resident.

Dr. G. Jessel raised the question of the value of mass radiography in tuberculosis, and it was resolved that Dr. Jessel should report at the next meeting on the rôle of mass radiography in tuberculosis.

The date and place of the next meeting were left to the officers, and Dr. D. P. Sutherland kindly offered the Council the use of the Tuberculosis Dispensary rooms in Manchester.

## REVIEWS OF NEW BOOKS

*Tuberculosis and Genius.* By LEWIS J. MOORMAN, M.D. The University of Chicago Press (Great Britain: Cambridge University Press). Price 15s.

From this book one can appreciate fully the peculiar influence tuberculosis had on the lives of some of our greatest writers. It depicts clearly that swift, feverish alliance between tuberculosis and genius, showing how a mental stimulus seems to be enhanced when the disease is at its height; how the "spark" is fanned by the haste of approaching death, by the frantic writing against time, and the growing realisation of the life-pattern. It calls to mind that poignant sonnet of Keats:

"When I have fears that I might cease to be,  
Before my pen has gleaned my teeming brain."

Dr. Moorman—himself a specialist of the disease—has given us an extremely interesting book. He has traced the influence of tuberculosis on the lives of Robert Louis Stevenson, Schiller, Marie Bashkirtseff, Katherine Mansfield, Voltaire, Molière, Francis Thompson, Shelley, Keats, and St. Francis of Assisi, devoting a chapter to each. Numerous references are made throughout to other famous writers who were also diseased in this way, and it is disturbing to see what a great number there are. The book, which is beautifully produced and written in a pleasing style, will interest the specialist and layman alike.

*The Report of the Medical Research Council for the Year 1938-39.* London: His Majesty's Stationery Office. Price 3s. net.

This report gives a brief account of the proceedings of the Council in promoting and financing research throughout the whole field of medicine, and it includes an interesting section on War Emergency Services.

Two problems related to tuberculosis have been studied: the National Institute for Medical Research is investigating the solid P.P.D. form of tuberculin with a view to the adoption of a new international standard for this substance, and Dr. Stanley Griffith has completed his investigations of the bacteriological characteristics of tubercle bacilli occurring in the sputum of persons suffering from pulmonary tuberculosis. In addition, the Council has given financial help to a number of workers investigating single problems connected with tuberculosis.

*A Practical Manual of Diseases of the Chest.* By MAURICE DAVIDSON, M.A., M.D. Oxon., F.R.C.P. London: Second Edition, 1941. Oxford University Press, Humphrey Milford. Price 42s.

The first edition of this book was a notable contribution to the literature of pulmonary disease. It appeared when the time was ripe for a comprehensive survey of those many advances which had taken place since the last war, and when the need for an up-to-date textbook on the subject

was clearly felt. Davidson's book covered both these wants, and, in addition, it was written in an easy style and was most beautifully illustrated.

This second edition appears six years after the first, a period which has been fruitful in further advances. These are given full and proper measure, and mainly on this account the book enlarges by some fifty pages. Particularly the recent views on pulmonary collapse and its close relationship to the development of bronchial dilatation are given full consideration. Other instances are the changing views on cystic disease of the lung, the additions to our knowledge of the chronic pneumonias, and of the treatment of acute pneumonias with sulphonamides and oxygen. Although the book is primarily concerned with the medical aspects of intrathoracic disease, there is ample recognition of the importance of surgical investigation and treatment in those circumstances where it is appropriate, and the principles involved are fully discussed.

Readers will find this new edition as up-to-date as its predecessor, and it is a reliable guide to the most experienced English opinion in the field with which it deals.

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## NOTES AND NOTICES

THE Central Council for the Care of Cripples announces that the Trustees of the Lord Nuffield Fund for Cripples, which is administered by the Central Council, have recently made important grants to two of the leading Cripple Training Colleges to enable them to expand to meet war-time requirements. A grant of £12,000 has been made to the Cripples' Training College, Leatherhead, which will enable it to expand to 250 beds, and a grant of £10,666 to the St. Loyes Training Centre for Cripples, Exeter, to bring the number of beds there to 200. The final scheme at both Colleges will include provision for physical rehabilitation, vocational training and production of supplies of national importance. Both these Colleges already provide short-term training courses for the physically handicapped. At Leatherhead there are courses in light engineering, electric and oxy-acetylene welding, machine drawing, etc., and the syllabus is particularly suited to the requirements of machine tool making. At St. Loyes there are workshops for watch and clock and precision instrument making and repairing. Skilled work is being done for Government departments, and there is urgent demand for expansion.

Apart from the production side, these Colleges are ready to fulfil an important function as rehabilitation centres for war casualties, for which they are well suited, and a pioneer Occupational Therapy Centre has already been opened at St. Loyes, in close co-operation with neighbouring Emergency War Hospitals, which is already functioning to capacity for the benefit of orthopaedic wounded.

## UROPAC (IODOXYL)

We are informed by the makers of Uropac, Pharmaceutical Specialities (May and Baker) Ltd., Dagenham, that Uropac, in addition to 20 c.c. ampoules, is now supplied in 3 c.c. ampoules and in the form of a special solution for use in retrograde pyelography. Uropac is a contrast medium for use in intravenous urography, retrograde pyelography, and other radiological investigations. The new 3 c.c. ampoules, issued for the convenience of the operator in using the small quantities required for the treatment of children, are available at 2s. 6d. The solution for use in retrograde pyelography is supplied in ampoules of 10 c.c. at 3s. 6d.

We are also informed by the makers that the 20 c.c. ampoules of Uropac have now been reduced to 10s. 6d.

## THIAZAMIDE (SULPHATHIAZOLE)

A copy of the first edition of a pamphlet on Thiazamide has been sent to us by the makers, Pharmaceutical Specialities (May and Baker) Ltd., of Dagenham, England.

Thiazamide, which has recently been made generally available, was introduced for clinical trial under its laboratory number "M. and B. 760". It resembles Dagenan (M. and B. 693) in chemical and physical properties. The anti-pneumococcal and anti-streptococcal activity of Thiazamide is slightly lower than that of "M. and B. 693", but in staphylococcal infections Thiazamide is claimed to be the rather more active of the two. It is also better tolerated than "M. and B. 693" and provides an alternative chemotherapeutic agent for use in gonococcal, meningococcal, pneumococcal, and other infections.

The pamphlet gives details of the *in vivo* and *in vitro* activity of Thiazamide against a number of micro-organisms, and includes particulars of clinical indications, dosage, absorption, and excretion.

## THE CENTRAL COUNCIL FOR HEALTH EDUCATION

This Council is specially recognised by the Minister of Health as a vehicle for health education and propaganda. It has representatives from Local Authorities and specialists in presenting health material to the public. During the last year an Emergency Committee, under Dr. Charles Hill, was set up to deal with current problems, and at the special request of the Minister has started a complete programme of health education in the London air-raid shelters. For the present this is confined to London, but later it can be extended to other parts of the country.

The Committee meets for a weekly sitting, and has drawn up a number of carefully written popular leaflets and posters which are available through the Local Authorities. They have proved more popular than such pamphlets generally are, and are now being widely used.



In addition, a campaign of lectures and cinema demonstrations is now under way. A film introduction is being made by the Minister himself, and a programme of health films, judiciously blended with entertainment and instruction, is now being given in from ten to fifteen separate shelters each week in the London area. Far from accepting the present difficult conditions as a restriction of its work, the Emergency Committee has regarded them as a stimulus, and intends to go on meeting new needs as they arise. The address of the Council is now at Tavistock House, Tavistock Square, W.C. 1 (Telephone, Euston 2111), and the General Secretary, Mr. John Lee, will be glad to hear from Medical Officers of Health.



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